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THE AMERICAN
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EDITORIAL

THE AMERICAN SYNTHETIC CHEMICAL INDUSTRY.

Born of necessity, reared with much difficulty, and just reaching the stage where its knees were strong enough to sustain it, the infant American Synthetic Chemical Industry is threatened with an affliction which may lead to its early demise. It needs no learned prognostician or diagnostician to point out the nature of the oncoming ailment or to realize that quick means need be taken to fortify the patient against the attack.

Before the onset of the great World War there had been poured over this country a vast avalanche of tar synthetics, most of them designed to become permanent elements in the physicians' *armamentaria* for fighting disease. Many of them possessed distinct merit, and had created for themselves an unquenchable demand. The majority of them, however, were foisted upon the credulous doctor, for the good doctor has well earned this title, and for all practical purposes were merely makeshifts and only valuable as providing means for the astute German to unload some valueless by-products of tar for which his chemist could find no other avenue of sale.

It is said upon good authority that "once upon a time" a certain German firm found itself hampered with a fairly large consignment of a crystalline coal tar compound for which it could find no earthly use. A clear-visioned and not too scrupulous chemist, knowing that the compound was relatively harmless, advised packaging the article in 10 gramme units, assigning to it a sonorous chemico-therapeutic name and sending it over the seas to cure American migraines. Accordingly so was it done and the firm was promptly

cleaned out of its encumbrance and relieved of all worry as to the disposition of any such future accumulation of worthless by-product.

We are not enthusiastic about the correctness of the foregoing premise, but correct or not, it most certainly carries the message with it that America was a profitable dumping ground for an endless array of worthless therapeutic agents of this type, whose vogue ran parallel with the extensiveness and intensiveness of their advertising and soliciting campaigns.

The war, however, closed the ways to all of these synthetics, good and spurious alike, and America, who had given the Germans and others an unopposed right of way in the manufacture and exploitation of such remedies found itself denied of many articles of real therapeutic merit. So great had been our dependence and so complete our indifference that during the early part of the war such common substances as acetphenetidin, antipyrin, resorcinol, acetanilid and hydroquinone were marketed at ridiculously high prices and much distress was occasioned through the scarcity of other products of marked remedial value, such as arsphenamine and diethylbarbituric acid. American enterprise soon found a way out, however, and both in the matter of synthetic drugs and dyes quickly approached a season when independence of Germany was an assured fact. Quite naturally our joining in the fray made more insistent demands upon our industries and particularly upon the chemical industry which bore the burden of the work of supplying the high explosives and warfare gases. Indeed so great was this demand that the infant synthetic chemical industry quickly grew to a healthy condition. Augmented by those other factors the drug supply soon became large enough to supply the demand and prices reached a scale lower than ever before, particularly the prices of many of the synthetic patented drug products, the sale of which had previously been a German monopoly.

It is granted, of course, that the infant industry waxed strong and hearty in the absence of active competition. Now, however, the ratification of peace with Germany, where most of these synthetics had their origin finds that country making ready to bid again for a market for both their good and bad products.

This is where our infant industry may find its agent of destruction unless the antitoxin of encouragement be used to combat this factor. This country should undoubtedly provide for the manufac-

ture at home of all of the worth-while remedies and means should be found, despite foreign propaganda, to protect this industry in every possible manner.

Physicians should be on their guard against vicious and guileful propaganda directed against American products and pharmacists should insist upon buying and using American-made synthetics whenever possible.

Proof positive of the assembling of arms for an active campaign to re-establish the sale of German-made products is seen in the following paragraph taken from the *Munchener Medizinische Wochenschrift.* August 26, 1921 (through *Jour. Amer. Med. Assoc.*):

"The firm of E. Merck (Darmstadt) has had a unique film prepared which gives a survey of its various forms of activity. It is to be used in advertising in foreign countries the German chemical and pharmaceutical industry. Excellent pictures are produced not only of the buildings of the extensive plant, but also of scenes in the various factories and machine shops. Beginning with the raw material and leading up to the finished product ready for shipment, the manufacture of the most important drugs is shown; also the methods of producing therapeutc serums, with a glimpse at the enclosure in which the animals needed are kept. The onlooker gets also an insight into the work of the mercantile departments. Before the film should start on its world journey, it was shown in Darmstadt, August 14, to a circle of invited guests. The very interesting production, which consists of five parts, required an hour and a half for its exhibition, without oral demonstration."

Here is food for thought and reasons for this editorial message. I. G.

ORIGINAL PAPERS

ADDRESS OF FRANCIS P. GARVAN,*

PRESIDENT OF THE CHEMICAL FOUNDATION.

That the cause and the chief lesson of the World War was most truly appreciated by Pasteur when he said: "Science is the soul of the prosperity of nations and the living source of all progress—what really leads us forward are a few scientific discoveries

*Delivered before the joint session of the Society of Chemical Industry and American Chemical Society, at Columbia University, September 7, 1921.

and their application," was pointed out by Francis P. Garvan, President of the Chemical Foundation, who appealed to the chemists of this country to accept the responsibility for teaching the people of this country this truth as applied to the critical chemical situation of the nation.

"The people of the United States are ninety-nine per cent. right at heart and appreciative," he declared. "So are the people of England and of Canada. Their appreciation of chemistry must no longer be deferred in the terminology of the propaganda of foreign hostile interests, seeking only their destruction. Your work must never again be allowed to cease in the laboratory."

After describing the discovery by the English chemist, Perkin, of the basis for the subsequent development of the coal-tar industry and practically all organic chemistry, Mr. Garvan told how "the German, Hoffman, put this discovery in his bag and took it back to Germany," where "almost instantly he was able to make German industry, German universities and the German Government realize the importance of that bag."

"Immediate success led to a greater appreciation of an ever closer alliance of science and industry and an ever closer alliance between science, industry and the militaristic state," he declared. "This triple alliance changed Germany from an agricultural nation into the second industrial nation of the world, but in that change, it brought about a succession of periods of over-production, each one in turn overcome by greater consolidation, by ever increasing corruption in methods of bribery, espionage, dumping, *et cetera*, and by ever intensified state aid and direction. In 1914, we find the German people demanding the control of the markets of the world. We find their hearts corrupted by the methods which they had felt it necessary to adopt to overcome their successive periods of over-production. We find them swollen with pride at ther successes and ready to inspire or acquiesce in the hazard of battle. This triple alliance of industry, science and the militaristic state—and the evidence is overwhelming that each was equally guilty—considered that it would be quicker and cheaper to attempt to gain this end by victory on the field of battle, rather than to find increased markets for a surplus production by further intensified methods of peaceful penetration.

"The same chemical research with its well-served industry had

in turn well served the militaristic state. As chemical progress indexed commercial progress, so explosives had kept pace with dyes and pharmaceuticals, the ammunition factories of her peaceful penetration were the arsenals of her munitions preparation.

"In the fall of 1913, the chemical application of Perkin's discovery was able to notify the war lord that Germany was ready; that she controlled 95 per cent. of the organic chemistry of the world, upon which industry and the production of war gases and explosives were dependent; that she had crushed out every incipient effort toward the development of the Perkin discoveries by every other nation and was able to deal the dependent industries of those nations tremendous blows, and that now by the final triumph in the development of the Haber processes of making nitrates from the air, her agricultural production and munition production were safe from the menace of ony blockade. You know the rest.

"All this German chemists accomplished not alone in their laboratories, but in the forum of public opinion. They had educated and moulded thought in Germany until every man of whatever rank, in or out of industry, education or governmental service, realized the importance of chemistry in his life and in the life of his country. They knew that the alliance of science and industry had increased the wealth of the world a thousandfold in the past hundred years. They knew that it was the life blood of industry; they knew it was the safety of their state and the only sure foundation upon which to base the hope of the health of their children's children, and they had impressed upon the world the discouraging and withering idea that the Germans and the Germans alone were mentally equipped to lead in this great age of chemistry."

As an instance of the foresight of German chemical interests, Mr. Garvan told how "prior to 1908 German patent laws contained the so-called working clause, by which your inventions, if patented in Germany, must be worked there within a certain period of time or they were thrown open to the German manufacturers and developers. Agitation was rife in this country that we should protect our future in like manner. But by 1908, Germany had decided that she had so far advanced in science that she no longer needed that clause to protect herself and that if enacted by the United States, it would threaten her control of organic chemistry in the world and destroy the purposes upon which she was bent.

"The President of the Bayer Chemical Company, at that time the head representative of this march for world control in America, although on paper an American citizen, acting under instructions from the consolidated government and chemical industries of Berlin, went to Commissioner Moore at the Patent Office in Washington. It was the beginning of one of Washington's hot summers. With fulsome praise of his outstanding position in the patent world and the great inventive genius of this country needing protection, he reproached him for not representing the United States at the International Patent Conference about to be held in Stockholm. Mr. Moore responded that the unenlightened Congress had not given him any funds with which to go. Mr. Moore then went on his vacation. Mr. Muurling, the predecessor of Schweitzer and Metz as the American voice of Germany's chemical interests, went to Robert Bacon, then acting Secretary of State, drew the picture of the United States unrepresented at that great conference, pointed out to him that he had a fund which he could apply to any purpose which he deemed for the best interests of the country in its foreign relations, with the result that Mr. Moore was recalled from his vacation and sent abroad, but with him went a letter to the German chemists, telling them that the American representative of the German dream had done his part and that they must now do theirs.

"The result was that Moore was induced to go from Stockholm to Berlin, where he was feted and dined by the Kaiser himself and returned to negotiate the treaty of 1909 with Germany, by which Germany was released from ever working her chemical patents in this country and by which the last hope of development of organic chemistry in this country was crushed. No more loyal Americans ever lived than Robert Bacon and Commissioner Moore, but they were unconscious tools in the hands of the German chemists, the handmaidens of the German dream of world control. And you were to blame because you had not instructed your government officials up to a realization of the importance of chemistry and its guidance and protection by the State."

"In Germany today industrial reorganization for world domination first in the peaceful arts and then in war is proceeding mightily under the sympathetic eye and fostering care of a government which differs in no important particular, so far as the world outside of Germany is concerned, from the government of the Hohenzollerns,"

said Mr. Garvan. "The German purpose stands forth as clearly as a mountain in the sunlight. First, reconquer in industry and commerce, then we Germans will see. Their secret documents prove it. The heart of the news that comes out of Germany proves it. They prove it out of their own mouths.

"Moles in the darkness, German agents in America are once more plotting against our security, our prosperity and against the health of our very children. The German design to render the United States important is being prosecuted today with more subtle viciousness than marked the intrigue of Von Bernstorff, Dr. Albert and Hugo Schweitzer in the years before we entered the war.

"The times are too tense with danger for passive tactics. On one side we have the same old crowd of German agents masquerading as good Americans. On another side we perceive American citizens supporting the German intrigues. In Congress we hear and stand aghast at the ignorant and malicious outburst of certain legislators, unmindful of their country's welfare. Folly drips from their mouths. Stupid suspicion of the motives of honest men and appalling ignorance of the times mark their astounding incapacity. There are some, who, like Jacob of old, have set themselves to steal the birthright of chemical independence from the American nation. They may disguise for a time the hairy hands of the German dye monopoly that controls them, but in the end the people will know them for what they are. Their voices are the voices of elected Representatives and Senators in the American Congress, but the hands that manipulate them are the hands of the German dye trust, the most powerful monopoly ever formed by man, the Interessen Gemeinschaft, the 'I. G.'

"If, in the reaction of war and in the general distaste for discussing matters pertaining to war, we permit ourselves again to be lulled and numbed by German propaganda, if we look on indifferently while a few demagogues in Congress and a few short-sighted, selfish men in business life play the German game, if we allow Germany to stifle an American industry that would within a very few years make the United State absolutely safe, then, I say, it will have been through your neglect and temerity and failure to realize that it is your responsibility not only to search the truth, but to preach it.

"Your responsibility today is the same as it was during all these

years of neglect, only intensified as it must be by your consciousness of the results of that neglect. You have listened without apparent protest contenting yourselves with resolutions and telegrams to swell the waste paper baskets of Congress, to the German lie that there was a 'Dye Monopoly' in this country, or that such a monopoly would result from the enactment of a selective embargo, when you knew that the development of a dye industry is synonymous with the development of education in organic chemistry and that no monopoly in education is possible without the compulsory partnership of industry, university and government, such as exists in Germany. (A monopoly which never worries those tools of German propaganda.)

"Did it not bring in your minds the lessons of the war when you saw the importing representative of the German 'I. G.' stand on the floor of the House of Representatives, flanked by fifteen of the seventeen Congressmen who voted against the declaration of war, leading the cheering when the first great unsuccessful test came as to whether American chemists should be given a chance to catch up their neglect of forty years and atone for it by leading this country through the development of organic chemistry into the realms of intensified national industrial progress, secret security to home and child and blessed advance in the medical service of humanity? Do you not feel that the voices of two German importing firms were louder in protest and more persistent in their appeal for Germany than the voices of your fifteen thousand members for America's lessons of the war?

"Again I repeat, Herman A. Metz stood upon the floor of the House as that vote was announced and shouted to a gallery of American citizens, 'I've got you licked.' And when he screamed in triumph, he meant 'I, the representative of the Interessen Gemeinschaft, the 'I. G.,' the combination of German government and German chemical industries; I've licked the advice of your General Pershing; I've licked the advice of your Secretary of War; I've licked the advice of your Secretary of Navy; I've licked your President; I've licked your Administration; I've licked your thirty million dollar investment in your colleges; I've licked your chemistry in your high schools and your public schools; I've licked your research institutions and the future development of medicine in America.' "

After outlining the development of the peace idea and the progress of war weapons up to the discovery of war gases, Mr. Garvan said:

"These things hit at the heart of imagination, surveying what creative chemistry has already done in war in its first few experimental steps, we stand back impressed as never before in the whole history of war tools. We are bound by sheer intelligence to comprehend that chemical science 'has only begun to fight.' It has learned how to utilize, not very skillfully, a few gases. It has not done anything beyond small scale experimenting with radio active forces. But the lessons of the great war were a tremendous impulse to the research chemist. The creative chemist is searching out among rare elements, such as radium, arguments against warfare that can no more be refuted than pigmy man can oppose the tornado, or the earthquake, or contend with Vesuvius. The strange stuff that illuminates the dials of our watches may be the very medium that will eventually produce the resistless force that will make fighting intolerable.

"Chemists are seeking through forces as yet imperfectly comprehended to turn man toward sanity. They are aiming at his imagination. Who will dare say they are pursuing a fruitless quest after the experience of the great war which began as a war of great steel projectiles and ended as a war of invisible energy. Hard-headed military men, usually slow to convince that weapons other than the traditional arms of their service must be learned and relied upon, join nowadays with chemists in an appeal to the public understanding which is little short of the striking appeal made by the imaginative story of Mr. Wells, for they realize that chemistry is merely on the brink of great things, and none see so clearly as they that chemistry aims to abolish war by making it desperately perilous to great nations as well as small, to governments as well as to the led peoples; to vainglorious politicians as well as to the obedient servants in uniform."

Following a description of Dr. Hugo Schweitzer, as a chemist, scientist and researcher, a German spy, secret service number 963,192,637, head of the German Secret Service in America, head of the system by which every effort to develop the organic chemical industry in this country was crushed out, head of the system of dye

salesmen by which every fact and circumstance of the four billion dollars a year American dependent industries was reported to Berlin, carded and charted there, taken into the great industrial establishment at Grosser Lichterfeld, outside of Berlin, and there placed at the disposal of competing German industry; the inventor of the idea of the purchase of the *New York Evening Mail* to corrupt our information; the inventor of the idea of the German Publication Society, formed to publish for our delectation the literature of German Kultur; head of the chemical exchange, by which all available phenol supply in America was turned away or made inaccessible to the Allies," Mr. Garvan concluded:

"Gentlemen, personal responsibility is a thing that cannot be escaped. We may go to our graves, but there will come forth from the unforseeable transmutations of destiny or from the divine will, some reaction of our unconsidered acts or of our deliberate evasion of the moral law that may cause misery to a multitude.

"Two years ago there leaned against a lamp-post on the Bowery, a strange Jew, with only his landlady's borrowed quarter in his pocket, only hate in his heart and wrong-thinking in his head. Today this man, Trotzky, controls the destinies and happiness of three hundred millions of Russian men, women and children. He, the mouthpiece of false ideas seized upon the ignorant and desperate mass in the hour of their agony, and has proved their destruction. Contrast his unwholesome and blasphemous career with that of Joan of Arc, who has always seemed so human, so natural, so close to all of us, her sweet, simple, girlish figure, sublime in her faith, sustained in her virtue and mighty in the power of her dominant will and the justice of her cause. She has been with us now for hundreds of years and never more so than during this war when she staunched the heart of France and led her brave as of old. As it is with these two individuals of humble origin, so it is with the highest. Contrast the Emperor of Germany, in whom self-love and ambition had crushed out all spirituality, leading his people and forcing them on in the conquest which has brought such unspeakable misery and suffering to untold millions of men, women and children—contrast him, I say, with that magnificent figure, Cardinal Mercier, that soul of resistance to injustice and falsehood, whose memory constitutes a solace, stored up for the distressed people of all future times.

"As it is with the lowly peasant man or woman, as it is with the emperor on his throne, or a prince of the Church, so it is with the scientist or the researcher. Contrast the influences intended by Perkins, who, at the end of his life, received his richly earned honors with bowed head and in humble voice: 'What is it that I have not received? Not unto me, O Lord, not unto me, but unto thy great name be all the praise.'

"Contrast him, I say with Schweitzer, the scientist and researcher, representative of the profane application of his science in peace and war, and in the shadow of that contrast, and in the humility and in the shame which we should feel, let us look forward to the day when the English and American chemists can meet again, with the evidence about us of our atonement for our neglect, evidence of permanent peace in all the world, of a higher and more equal standard of living for all our peoples and of a great marching forward in our battle against disease. Until that day let no man write his epitaph."

METHYL-ORANGE AS AN INDICATOR IN PRESENCE OF INDIGO-CARMINE.*

By Professor Frank X. Moerk.

Methyl-orange used with the more dilute or weaker volumetric solutions for accurate work should be compared with a blank test to correct for its alkalinity and also to reduce error because of the gradual color change.

In a pamphlet issued in 1914 by the Wilckes, Martin Wilckes Company, of New York, on "Methods for determining the strength and impurities in Acid Calcium Phosphate" a formula is given for preparing an indicator for the "determination of free phosphoric acid" by the use of which the change in color is more sharply distinguished; 25 cc. of a solution of Methyl-orange (1:1000) are mixed with 5 cc. of water containing 0.09 Cm. of sodium sulphindigotate (indigo-carmine).

Looking up the literature of this mixture as an indicator, *Chem. Abstr.* 1908, page 165, gives reference to an article published by R. Luther in *Chem. Ztg.*, 1907, page 1172, in which priority for the

*Read before meeting of Pennsylvania Pharm. Asso. June, 1921.

*Chemical Laboratory Philadelphia College of Pharmacy and Science, June 10, 1921.

combination was claimed quoting an article by J. A. Af Hällström in *Berichte,* 1905, page 2288.

The several original articles in the order of their publication contain the following information:

(1) J. A. Af Hällström in an investigation found it necessary to determine alkaline carbonates and bicarbonates in presence of phloroglucin; as the solutions were always colored, the titration with HCl V. S. (ethyl-orange indicator) was unsatisfactory. Prof. R. Luther, under whose direction the investigation was made, suggested the addition of indigo and this then enabled more satisfactory titrations.

(2) C. Kirschnick in *Chem. Ztg.,* 1907, page 960, published an article under the title of "Indicator for the determination of free acid in zinc chloride solutions, etc." The demand for an indicator which combined the sensitiveness of methyl-orange with a better end-reaction in turbid or light-colored solutions induced the author to bring about a change in color of the methyl-orange solution. It was found that an addition of indigo-carmine under certain conditions of dilution produced a pure green color which by the minutest addition of normal acid changed to a violet-red. The following dilution proved practical: One gram of methyl-orange and one gram of indigo-carmine were each dissolved in one liter of water; 20 cc. of the methyl-orange and 60 cc. of the indigo-carmine solutions were mixed and diluted to one liter.

This mixed indicator was used in testing zinc chloride in the following manner: 10 cc. of the indicator was diluted with 100 cc. of water and 10 cc. of the zinc chloride solution (25% Zn) added; an unchanged green color shows basicity, a resulting red color shows acidity of the zinc chloride; by titration, the bacisity or acidity of the salt can be determined. This indicator can also be used to determine the free acid in superphosphate. Pure indigotin dissolved in sulphuric acid and carefully neutralized can replace the indigo-carmine.

(3) B. Luther in *Chem. Ztg.,* 1907, page 1172, furnishes more information under the title of "On the addition of Indigo in titrating with methyl- or ethyl-orange."

"In the *Chem. Ztg.* 1907, page 960, C. Kirschnick recommends an addition of indigo in titrating yellow colored solutions with

methyl-orange. Two years ago J. A. Af Hällström upon my suggestion applied the same addition for the same purpose. As the intended detailed publication of this artifice was postponed until the completion of some additional experiments, a few statements may be communicated at this time.

"The addition of indigo to yellow colored solutions undoubtedly increases the sharpness of the end-reaction. But we must not forget that the quantity of indigo-carmine to be added must be proportional to the yellow coloration. The more intense the yellow color the sooner will appear the change of color from violet to green and so much later the change from green to violet. A definite formula for the mixture suitable for all degrees of yellow colorations is not possible. In case of approximately uniform yellow color solutions and, especially, in cases of somewhat concentrated solutions for titrations this condition need hardly be considered, as the addition of indigo-carmine allows titration which would otherwise be impossible.

"It appears to me that the addition of indigo-carmine in the accurate titration of colorless solutions with methyl- or ethyl-orange is of even greater value than in the titration of yellow colored solutions.

"To obtain distinct end-reactions in titrations with alkaline hydroxides containing carbonate the suggestion of Küster is followed by preparing a 'normal color' by saturating the methyl-orange solution with carbon dioxide and titrating to this color. As the changes in color, red, orange, yellow, especially in dilute solutions, are gradual the end-reaction may be doubtful. In these cases indigo-carmine is of advantage as its color is practically complementary to the 'normal color.'

"It is possible by a few trials to obtain the proper mixture of methyl-orange and indigo-carmine which will result in giving an almost neutral gray with carbon dioxide; sufficiently dilute solutions of such a mixture will then appear almost colorless.

"The change in color from violet, though colorless, to green is very pronounced and titrations in dilute solutions, especially, are more easily made; the end-reaction is colorless (gray.)

"As indigo-carmine with excess of alkali changes to yellow, the complete color changes obtainable in titrating an alkali with acid is as follows: yellow, green, colorless (gray), violet. The multiplicity of color changes has the advantage of preparing one for the approach of the end-point; overstepping the end is therefore, even in rapid work, easily avoided.

"Very few references in literature were found mentioning the yellow color produced by dilute alkalies on indigo derivatives."

The two formulas given above if calculated to a common basis will not agree; several other mixtures were made:

	Methyl Orange.	*Indigo Carmine.*	*Water.*
A	1.000 Gm.	3.6 Gm.	1000 Cc.
B	1.333 Gm.	4.0 Gm.	1000 Cc.
C	1.000 Gm.	2.5 Gm.	1000 Cc.
D (Kirschnick)	1.000 Gm.	3.0 Gm.	1000 Cc.
Wilckes	0.833 Gm.	3.0 Gm.	1000 Cc.

0.2 cc. of D diluted to 100 cc. will duplicate the strength recommended by Kirschnick. The first four solutions (C and D preferentially) were used for experimental purposes and were found to give uniform results in titrations with tenth-normal volumetric solutions if the following details were observed:

Dilute two portions of 0.2 cc. indicator with 100 cc. of water and add to the green or greenish-yellow solutions just enough acid volumetric solution to discharge the yellow or green color without producing a red or violet color; should the latter color show add enough alkali to discharge it. The object is to produce a "neutral tint" showing neither alkalinity nor acidity; disregard the volumetric solutions necessary to accomplish this.

Reserve one of these solutions and to the other add the substance to be titrated; a violet or purplish color indicates an acid substance, a yellow or green color indicates an alkaline substance. Titrate with an alkali or an acid volumetric solution, as the case may require, until the color matches that of the reserved solution. It is next possible to add to the reserved solution another portion of the substance to be titrated and check this against the previously titrated portion. The titrated solution will respond by color change with a single drop of acid or alkali volumetric solution.

A modification of this method was tried by taking in duplicate, 10 cc. water, 0.05 cc. indicator, then traces of acid volumetric solution to yield the neutral tint (which in this case is colorless); next add to one of the solutions the substance to be determined and titrate with acid or alkali volumetric solution to reproduce the neutral tint. As only a few titrations were made by this modification, preference is given to the first method.

The following substances were titrated in the course of the above work: Sulphuric and phosporic acids, sodium borate, carbon-

ate, hydroxide and phosphate. It should not be necessary to here state that the standardization of the volumetric solutions employed must be made by the same method.

Solutions are submitted to show changes in color of methyl-orange in comparison with the mixed indicators A and C, these illustrating the greatest variation in the quantities of methyl-orange and indigo-carmine.

EGYPTIAN SECRETS AND MAGICAL SPIRIT ART OF THE PAST AGES.*

By Edward J. Hughes, P. D.

The practice of witch-craft, the white and black art, voodooism, or hex-doctoring is considered by most people, in our enlightened age, as a reflection upon our intelligence. Yet it is surprising to find that only a few hundred years ago the treasured Egyptian secrets were highly esteemed and the magical spirit art was practiced by men of highest repute, such as priests, alchemists and philosophers. Then too, we are reminded by the newspapers that in our present day there are those who seek to find relief from their sufferings and confusion by the use of charms and incantations.

Needless to say, it is not the object of the writer to advocate the use of these weird hallucinations. Nevertheless it is interesting as well as amusing to examine some of the ancient literature and there find recorded the cure-alls that were in vogue at that time. Signed statements are made, apparently with sincere reverence, as to the efficacy of these remedies, and miracles are said to have been wrought by methods which to us may seem ridiculous.

One of the books dealing with the magical spirit art is called the Sixth and Seventh Book of Moses. The copy of this in English is said to have been translated from the German and that, in turn, from the ancient Hebrew. This contains a mass of incoherent material showing about as much connection throughout the text as one might expect to find in an ancient dictionary. It contains a lot of hieroglyphics, symbols, seals, magical formulas and incantations. Besides these it contains a collection of writings from both the old and new Testaments with many other sacred writings of doubtful

*Read at the Convention of the Pennsylvania Pharmaceutical Association, held in Philadelphia, Pa., in June of 1921.

authority. It is distinctly a book of faith cures. The last few pages of the book are devoted to astrological influences upon man and the magical cures of the old Hebrews. Among the latter are the following examples:

Diseases of the Eye:—The saliva of the first-born on the male side (not of the female side) is effective in the cure of eye diseases.

Fever:—Take a seat on a cross-road and as soon as you observe a large ant carrying something, take her up and place her in a copper tube. Close the opening with lead and seal it with sixty seals, shake the tube and hang upon your body and say to the ant: Thy burden upon me and my burden upon thee.

Another literary curiosity is found in the book of Egyptian Secrets by Albertus Magnus, revealing the forbidden knowledge and mysteries of the ancient philosophers. The statement is made in the preface that this book was issued for the purpose of rendering a great service to mankind and in order to bridle and check the doings of the devil. It is also claimed, by Albertus Magnus, that these secrets have been proven and found efficacious by those having the true belief.

The following list of examples taken from this volume gives a fair conception as to the nature of its contents:

For Bad Hearing. Take the oil with which the bells of churches are greased and smear it behind the afflicted ears and relief will not fail to come at once.

To Make Ones Self Invisible. You must obtain the ear of a black cat, boil it in the milk of a black cow, then make a thumb cover of it and wear it on the thumb and no one will be able to see you.

How To Be Able To See In The Darkest Night. Grease the eyes with the blood of a bat.

To Ascertain Whether A Sick Person Will Become Well Again. Cut a piece of bread, rub the patients teeth therewith, and throw it before a dog. If the dog eats it the patient will recover. Otherwise the disease is dangerous.

To Facilitate Healthy Sleep. Procure two rabbit ears, place them under the pillow of a person who cannot sleep, without his knowledge.

To Drive The Mice Away From Barns. Burn a rotten crab to powder, fumigate the barns with it and all the mice therein will die.

To Make The Hair Grow Wherever You Choose. Take dog's milk and paint the spot therewith wherever you wish to have the hair grow. It will surely grow.

To Make a Person Dislike Gambling. Speak to an executioner, give me some wood of a whip wherewith you have beaten criminals and flog the gambler with this upon his naked body. Nevermore thereafter will he gamble.

To Catch Fish. Take valerian or cocculus indicus and make small cakes therof with flour, throw these into the deep. As soon as a fish eats thereof it will become intoxicated and float upon the surface.

When You Hear Something Said That You May Not Forget It. Take the heart of a swallow, boil it in milk, and carry it on your person and you will remember all you hear.

The selection of the foregoing list is not designed to discredit the accomplishments of Albertus Magnus. History records him as one of the foremost of the medieval philosophers. He was known as the Universal Doctor in addition to being an astronomer, a theologian and an alchemist and knew practically all that was to be known in his time.

Not all of the secrets published by Albertus Magnus in this volume are of the same superstitious and somewhat magical character. Some of the remedies employed by him have passed safely through the centuries and are valued pharmaceutical substances and medicinal agents of the present day.

For instance, a splendid eye water is recommended composed of white vitriol, native camphor and rose water. Constipated persons are told how to open the bowels within one hours' time by taking a dose of salts and senna such as apothecaries sell. The value of astringents in stopping the flow of blood is utilized in a remedy for nose bleeding which directs that a little wadding be dipped in good ink and inserted into the nose or other bleeding injuries. An ointment for burns is recommended containing rosin, tallow, wagon grease, wax and turpentine oil. A blister plaster is found composed of cantharides, turpentine, yellow bees-wax and linseed oil. Another ointment for burns is directed to be made by mixing upon a coal fire two ounces of turpentine, three ounces of yellow bees-wax and six ounces of linseed oil.

For a time alchemy was associated with superstition in the hands of magicians and practitioners of the black art. We are told,

however, that the quackery and mysticism that did much to discredit alchemy during its later period were the products of an ignorant and superstitious age and the result of the inability to read and understand some of the ancient manuscripts.

The recent revelations of the extent to which the charms, incantations and queer ceremonies of witch-craft still flourish in some of the rural sections of Pennsylvania bears evidence that even today many people are following along the lines of ignorance and superstition and are calling upon the witch doctor for relief.

In one instance two verdicts, aggregating $15,000 in damages, were awarded to the father of two girls over which the witch doctor had acquired almost absolute control. On one occasion he bored a hole in a tree with an auger, clipped off the girls' hair and placed it in the hole, meantime mumbling mystic words.

The newspapers reported a case only a short distance from Allentown, Pa., where a man and his wife were shot because the would-be murderer believed that they had bewitched him.

Another interesting news item was to the effect that a witch doctor had been arrested in Reading, Pa., for having obtained money under false pretense. This was said to have caused a fine flutter among the best people of Berks County who feared that he might betray some of their family secrets.

The most fertile soil for the development of a belief in the efficacy of the black art, magical spirit art, quack doctors, witch doctors or any other form of pow-wowing is found in the mind of the ignorant and uneducated. Like the people of the dark ages their tendency seems to be to look to the supernatural, the magical and the mystifying. They are not acquainted with the facts so their efforts are bent toward creating a world after their own imagination. Books like the Sixth and Seventh Book of Moses and The Egyptian Secrets are interesting to us only as a matter of curiosity. Yet, it is impossible to calculate the harm that may be done by allowing them to fall into the hands of people of this type.

Our most effective weapon in combatting the evils that may arise from the indiscriminate use, at the present time, of magical cures and ancient secrets is found in our educational system. Every effort should be made to advance the standards of our country school in order that their influence may be as effective and as far-reaching as possible.

SMELL SHOCK.

RALPH R. FORAN, P. D.

Smell is the sense by which odors are perceived. We know that, in man, the organ of smell is the olfactory bulb, located at the anterior extremity of the olfactory tract of which it is an enlargement, the olfactory tract being a prolongation of the cerebrum. We further know that the development of this bulb bears direct relation to the acuteness of smell. But of the mechanism of olfaction we know very little. Various theories have been proposed to explain the why and wherefore of smelling, but all of them have largely failed to prove anything. It is one of the many unsolved riddles of life processes and we will have to take our first premise as a matter of faith.

The sense of smell is widely distributed throughout the animal kingdom. The lower animals, especially those breathing in water, become cognizant of the presence of odorous matter near them without touch, vision or hearing, and it is supposed that they do so by some sense of taste or smell, or a combination of both. Pharmacists may recall the sale of oil of rhodium, reputed by some fishermen to be an "added inducement" for fish which are otherwise shy of the bait. Most birds are probably without the power of smell, and in some, such as the frigate bird, the nostrils are obliterated. An instance is reported of three or four hens picking over a rubbish heap on which some calcium carbide had been thrown, and while the place reeked of acetylene the hens did not seem to mind it. Dogs, which are primarily dependent upon smell in their daily life, appear to be able to isolate a single smell component within a highy complex mixture. The fondness of cats for catnip, while unexplainable, is an indication of their acuteness of smell. In man the sense of smell is very feeble and imperfect in comparison with that of many animals, especially of the carnivores, which pursue their prey by scent, although it is declared that the half-savage Ainu of North Japan can track game like a dog, by the nose alone. James Mitchell, the English blind deaf-mute, recognized his friends when they came into a room, simply by their smell. Bucklan, the geologist, when riding once with some friends and the party lost their way and were overtaken by night, alighted from his horse, picked up a handful of earth, smelled it and at once declared they were near Uxbridge. He

knew the geology of the land and the smell of the soil. Generally speaking, however, the average man has limited olfactory power, unless he has improved the sense by exercising it.

In endeavoring to connect the sense of smell with the chemical constitution of the substance, Sir William Ramsay has pointed out that, as a general rule, substances having a low molecular weight have either no smell or simply cause irritation of the nostrils. He also shows that in the carbon compounds increase of specific gravity as a gas is associated to a certain point with a sensation of smell. It has also been pointed out that compounds of elements belonging to the same group, according to the periodic law, have sometimes odors of a similar character. But beyond this, there is no classification of odors. We must be content to describe an odor as pleasant, disagreeable, aromatic or characteristic and so on. This sort of description may mean anything or nothing, when it is considered that an odor may appeal to one person as being pleasant and to another as being obnoxious.

As to the intensity of odors, it is said that musk to the extent of only four one-hundredths of a milligram per liter of air is detectable and thus it is that a grain or two of musk will scent a room for years and at the end of the time no appreciable loss of weight can be detected.

As to the susceptibility of humans to odors, some persons may be sensitive to some odors while they do not recognize others. It is not uncommon for students to fail to recognize hydrocyanic acid in a solution given them for analysis.

The detection and identification of odors is of much importance to pharmacists and it was with the thought of determining their responsiveness that the following experiment was carried out. A series of fifteen liquid odorous substances was submitted to twenty men selected at random. Six of these men were members of the faculty of the Philadelphia College of Pharmacy, all of whom had had pharmaceutical training. Six were students with varying drug store experience and the remaining eight were graduate and practicing pharmacists. The purpose of the test was to identify specific odors and consequently color, taste and mobility were not to be taken into account. The substances submitted were as follows: Oil of turpentine, ethyl alcohol, oil of cinnamon, vinegar, oil of orange, kerosene, creosote, oil of sassafras, methyl salicylate, benzaldehyde, gasoline, ether, oil of anise, linseed oil and oil of nutmeg. The re-

sults of the experiment were both interesting and amusing. Oil of turpentine was recognized by all except three and these men called it in turn—oil of anise, oil of caraway and pine oil. Alcohol was difficultly recognized by the majority, a few claiming that it had no distinctive odor. One of the faculty of the College, after inhaling the liquid for several minutes refused to commit himself, although he said the odor was very familiar to him. Peculiarly, oil of cinnamon was reported as oil of anise, oil of bitter almond and oil of wintergreen by three of the contestants. Vinegar was easily recognized, although one of the men said that it reminded him of cheese. It was to be expected that oil of orange would be mistaken for oil of lemon and eight men reported the latter. The difference between the two is not very pronounced it is true, but to the trained nose is readily discernible. Kerosene and gasoline were confusing to quite a number, indicating that gasoline is not what it is "cracked up" to be. Why two men should report gasoline as chloroform is beyond explanation. Similarly, two men reported kerosene as carbon disulphide. Ten men judged wrongly on creosote. Five reported oil of clove, and the other five reported cresol. Those who were unsuccessful in identifying oil of sassafras and oil of anise, said that they recalled the odors as being those associated with salt water taffy. Only two men failed to identify methyl salicylate (synthetic oil of wintergreen), and singularly both of them reported oil of peppermint. Running true to form, benzaldehyde was twice mistaken for nitrobenzene (oil of mirbane). Only one man failed to recognize ether. He reported this as ethyl nitrite, at the same time reassuring himself by saying that he had worked with this substance at college while doing thesis work. Nine men were able to identify the odor of linseed oil. The others reported it variously as fish oil or cod liver oil and one said it was neatsfoot oil. The similarity of odor of linseed oil and cod liver or fish oil, is sometimes baffling unless the olfactory nerve is highly trained. The identification of oil of nutmeg was not attempted by three of the men, three reported oil of turpentine one reported it as oil of colander and one as oil of cardamom.

It is significant to note that the sense of smell in one of the students examined was almost nil. He admitted that he detected only the most powerful odors and that he never noticed the odor of hydrogen sulphide in the laboratory, although his desk was less than six feet away from the hood where this gas was generated and used

continuously. One of the men was suffering from a severe "cold in the head," and while generally an inflammation of the nasal passages deadens the sense of smell, this man made a score of eighteen out of the twenty. Also, another apologized that he "didn't smell very good."

We have something to learn from this simple test, and that "something" is that we have been neglecting the education of our nose. The identification of substances by the sense of smell is a thing which cannot be taught. It must be acquired by the process of exercising the function. Only "your nose knows."

TECHNICAL CHEMISTRY LABORATORY,
Philadelphia College of Pharmacy and Science.
June 10, 1921.

ABSTRACTED AND REPRINTED ARTICLES

A DREAM OF THE FUTURE.*

By E. SAVILLE PECK, M. A., Ph. C.

PRESIDENTIAL ADDRESS DELIVERED BEFORE THE BRITISH PHARMACEUTICAL CONFERENCE.

[The foregoing title may well be altered to American Pharmacy and its Possibilities and the dream which is so ably interpreted by Mr. Peck may also be the proper and happy aim of American pharmacy of the present day. Conditions related in this article are as vividly characteristic of our land as they apparently are of Great Britain and the remedies proposed for the correcting of these conditions should be quite as efficient for us and our calling as they are expected to be for our British conferes and their profession. —ED.]

On looking over the addresses of the distinguished pharmacists who have preceded me in this chair during the past few years, I find they can be roughly classified under four headings—those which deal purely with pharmaceutical science, those which have delved into the long-forgotten past, and endeavored from that rich field of

*From *The Chemist and Druggist*, 1921, pp. 46-50.

experience to extract lessons for the present, those which have reviewed the pharmaceutical problems which presented themselves for solution at the time, and those which sought to peer into the future and visualize things that might be or ought to be.

The purely science side has been so ably presented by my immediate predecessor that I feel it is unnecessary on this occasion to develop that aspect of pharmacy. As to what has gone before, I was sorely tempted to write of the deeds of "our fathers of old," but finally decided that it might be more profitable perhaps if I endeavored to point out some of the anomalies which exist at the present time, and then to give free rein to my thoughts and aspirations by outlining some the "possibilities of the future."

CONFINING DISPENSING TO PHARMACISTS.

There are several precedents for so doing; there was the address by Dr. Tocher at Newcastle, in 1909, on "Should the Dispensing of Medical Prescriptions Be Exclusively Confined to Pharmacists?" in which, after recognizing that it had been a practice from time immemorial for doctors to supply physic direct to patients, he showed that the total transference of the dispensing of prescriptions from medical men to pharmacists would be accompanied by advantages to the medical man, the pharmacist, and the public. As a result of this address a Conference was arranged with the British Medical Association, and took place on May 19, 1910. There was a long discussion upon medical dispensing, prescribing by unqualified persons, and the sale of secret remedies, and it was also decided to set up a Joint Standing Committee, consisting of representatives of the two bodies.

The following year, however, Mr. Lloyd George introduced his National Insurance Bill. It is interesting to recall the fact that the Conference, through its executive, took immediate steps to put forward the claims of pharmacy, and this Joint Committee when it met passed the following resolution among others:

That the principle be affirmed that the dispensing under the Government scheme be done through the channels provided by the Pharmacy Acts, and that provision be made in the National Insurance Bill itself for the carrying out of the Chancellor's expressed intention that this work should be done by pharmacists.

The annual meeting of the Conference confirmed these resolutions of the Joint Committee, but the Council of the British Medical

Association added to the resolution the words "or by medical men." No other meeting of the Joint Committee was held, and the work of securing full recognition of pharmacy under the National Insurance Act was carried on by the Pharmaceutical Society.

I have recited all this to point out that the Conference did, in 1909, 1910, and 1911, take action in the matter of confining, dispensing to pharmacists, and to assert that, in my opinion, the time is ripe for another attempt to be made to carry the matter a step farther; and now that the dispensing for a large class of employed persons has been largely settled by National Health Insurance, to secure that this sound and salutary principle shall be applied all round. The Pharmaceutical Society has recently made a very important move in this direction by drawing the attention of the Government to the fact that in the recent Kidwelly case of poisoning by arsenic the medicine supplied to the patient was not dispensed by a pharmacist.

PRODUCTION OF THE PHARMACOPŒIA.

At the Jubilee meeting in 1913 you will remember that Mr. J. C. Umney, after reviewing the methods by which the various pharmacopœias of the world are compiled, advocated the appointment of a Commission, to be called the British Imperial Pharmacopœia Commission, which should consist of medical practitioners, registered pharmacists of Great Britain and Ireland, the Professor of Pharmaceutics of the School of Pharmacy, and others, and that this Commission should have the exclusive right of publishing, printing, and selling the Pharmacopœia. This plan follows the lines of the production and publication of the pharmacopœias of most other countries, and it is high time that steps should be taken to bring this dream of the future production of the British Pharmacopœia nearer to realization, or at least to see that pharmacists are represented on the Pharmacopœia Revision Committee. If this matter of the Pharmacopœia is considered impracticable, and nothing but a dream, there can be no doubt that there is a general desire on the part of medical men and pharmacists for the early production of another edition of our own British Pharmaceutical Codex. It is agreed on all sides that this is a most valuable work and has enabled pharmacists and medical men to co-operate very closely in the prescribing and dispensing of useful combinations of drugs to the mutual advantage of patients, medical men, and pharmacists.

PHARMACY IN THE ARMY.

In my address in 1915 I advocated the formation of an Army Pharmaceutical Service Corps, somewhat on the lines of that obtaining in many of the Continental armies. In this connection I may be permitted to state that the Army Council, in December, 1920, invited the Pharmaceutical Society to appoint three of its members to represent the Society upon a Joint Committee with the Royal Army Medical Corps, this Committee "to consider the employment of pharmacists in the Army in connection with the supply, distribution, and dispensing of medical and surgical supplies in peace and war, and to make recommendations regarding their organization and status." That Joint Committee, upon which I have the honor to serve, has met on several occasions, but has not yet presented its report, and its findings are still confidential. As one of the representatives, I should, however, like to say that I consider sufficient progress has been made to justify me in thinking that a marked and much-needed advance in the position of pharmacists in the Army will result as a consequence of the work of that Committee.

RESEARCH WORK.

Then, again, in 1919, Mr. Kirby in his address showed us the necessity for placing pharmaceutical research on a sound national footing, and, as you will see in the annual report, steps have been taken to place this matter before the Ministry of Health. These four addresses upon research, pharmacy in the Army, the British Pharmacopœia, and the question of dispensing may be considered by some to be but empty dreams and vague imaginings; but surely we may look upon them, if not as probabilities, yet at least as "possibilities of the future." Now, these addresses were given to gatherings of pharmacists and those interested in pharmacy, who were met together in conference primarily to advance pharmaceutical research and to inculcate and uphold a high standard of purity in medicines.

This Conference has no executive power such as that of the Pharmaceutical Society, and in this very fact lies at once its strength and its weakness. Its President for the time being is therefore entitled, and in fact it is expected of him, to throw out hints and make suggestions as to the aims and possibilities of pharmacy, and I intend

to take full advantage of this opportunity and venture to put forward ideas which doubtless some, to quote Tennyson, will consider

"Wide of the mark e'en for a madman's dream."

DEPRECIATING PHARMACY.

My dream, for such it may be considered, is of a time when pharmacy in this country shall, as has so long been the case on the Continent, have established itself as a separate professional entity—a distinct career—not merely as a handmaid to medicine, but as a calling collateral, co-existent and interdependent with medicine. Pharmacy as a distinct craft, calling, or profession has not yet materialized as have medicine, law, and accountancy. There is need for greater publicity as to the education and qualification required of the pharmacist and the functions pharmacy has carried on for many years with credit to itself and for the public safety.

This need of publicity is clearly seen in the much-discussed Dangerous Drugs Act Regulations. If the functions of the pharmacist had been more widely understood and appreciated, it is inconceivable that the Home Office should have suggested regulations for the sale and dispensing of scheduled poisons which are in themselves a redundancy and already very largely covered by the Pharmacy Acts.

Let us consider how pharmacy is visualized by "the man in the street." In the main I suppose one must grant that he would look upon the pharmacist as the man who runs a chemist's shop or dispenses medicine in a public institution, and would consider that those practicing this calling are not to be looked upon as men of education or of professional standing. There may be some ground for this point of view; but there are well-known exceptions, and many instances can be cited where individual pharmacists have achieved coveted positions in the scientific, archæological, polical and municipal worlds. This has been due to the work that has been done by many outside their pharmacy and not because of their pharmaceutical qualification.

I recall an instance where a pharmacist read a paper of archæological interest at a meeting of a learned society after which a lady was heard to inquire: "Who is this Mr. X?" "Oh, don't you know he's Mr. X, the chemist." "Dear me, I thought he was a gentleman."

In the Army, notwithstanding the fact that the war was a great

"leveller," the same attitude was sometimes shown. I know of a case where an officer, who had all the qualifications necessary to fill a certain post but had in addition that of a pharmaceutical chemist was turned down, as he was informed, practically on this account. I do not consider this depreciation of pharmacy is due entirely to the fact that the practice of pharmacy is for the most part carried on "behind a counter" in "an open shop," but because the calling is so very "mixed"; it has many of the disadvantages of a profession and yet lacks the essential advantages of a trade.

IMPROVING THE STATUS OF PHARMACY.

I do not intend to be inveigled into an endeavor to differentiate between a trade and a profession, nor to affirm that one is more worthy, desirable, or honorable than the other. It can well be said that many so-called professional men carry on their profession in a purely commercial spirit, while many so-called tradesmen bring professional instincts to bear upon their business. Now, are we to be satisfied with the present condition of things and our existing standing in the public estimation? Do we wish to have the circumstances altered, and, if so, are we willing to purge ourselves of those things that militate against improvement, and also to put into operation certain influences that will make for greater efficiency and a higher position for pharmacy in the social scale?

Of course it is an essential consideration, which must precede any attempt to raise pharmacy to the status of a scientific and professional entity, that pharmacists must themselves wish for the elevation of their calling. Do they want to be recognized as possessing the technical knowledge and "competent skill" requisite for the practice of a profession, or would they rather simply draw their reward from protected profits on packed medicines? It is mere folly to complain, as some are apt to do, that pure pharmacy does not pay and leave it at that. It never will pay until it is acknowledged as an indispensable factor, with medicine in the nation's system of public health administration; and it never will be so acknowledged unless the will of the pharmacist is in and behind the movement.

One can do nothing for the men who want nothing and have no aspirations, but the possibilities are unlimited if the members of our calling really desire that pure pharmacy should be made to pay. I do not despise commercial acumen in pharmacists, and have

never condemned the "keeping open shop," but I do want to see it made possible for the pharmacist to make a living by pharmacy in that open shop, as well as elsewhere, and by virtue of his qualification, and not be forced to rely upon activities which do not call for a qualification at all. Shall we be content in the future merely to keep open shop and continue to carry on a purely commercial pharmacy, or shall we not combine in demanding an adequate remuneration for services dependent upon technical knowledge and competent skill and warranted by virtue of qualification? For those who have the necessary education, aptitude, and desire, should we not endeavor to carve out a more distinctly professional career? The scope of such a career could include the work of clinical pharmacists or clinical analysts, on the lines suggested for the Health Centres, of research workers in the large wholesale firms, and of teachers in the approved schools of pharmacy.

TWO CLASSES IN PHARMACY.

The question of the differentiation of pharmacy into two classes has for several years exercised my mind. I fully admit that, and that the subject bristles with difficulties and the magnitude of the task is obvious even upon superficial consideration.

To begin with, there is the difficulty of drawing a clear line between what is commercial pharmacy and what is clinical or professional. There is the training and examination essential for the one and unnecessary for the others. Then there arises the point as to where the differentiation as far as qualification is concerned should take place. In other words, where shall the differentiation between the business of a chemist and druggist and the profession of pharmacy come in?

On the Continent the division is made between those who can only sell drugs and certain poisons, and those who can be entrusted with the dispensing of medicines and physicians' prescriptions—with the addition in some cases of clinical analysis. In this country such an arrangement would not, I consider, at the present time be practical politics. The vested interests in dispensing are far too great, and, moreover the training required, and the standard of the examination demanded to qualify as a chemist and druggist, is probably sufficient for the duties he is called upon to perform at the present time. But there is the Major examination which could be extended

so as to include subjects which would cover clinical analyses, and the training for which would enable the student to undertake this work. The differentiation could take place here with less difficulty and disturbance than anywhere else—that is, because those who pass the Qualifying examination and those who elect to proceed to the Major examination and qualify as pharmaceutical chemists. I shall go more fully into this point later in my address.

CLINICAL ANALYSTS.

Here I would remind you of the report of the Consultative Council on Medical and Allied Services, which indicates that it is proposed that a Committee shall be appointed to investigate and report upon the question of what should be the future functions of pharmacists in relation to the services the Council were devising, and as to the most appropriate training and qualifications for those who are to perform these functions. In Section VI of this report it is stated: "It is a matter for consideration whether in certain cases, at any rate, individuals might not combine the duties of the pharmacist with those of the laboratory assistant."

This leads us to consider whether there is room for such trained men apart from the proposed Primary and Secondary Health Centres. Does the average general practitioner need the assistance of a trained clinical analyst to aid him in diagnosis and subsequent treatment? Would there be sufficient demand for such work in towns of, say, over 50,000 people to warrant the pharmacist in acquiring the requisite knowledge and setting up the necessary bacteriological and chemical laboratories for this purpose? I think there is room for such a development, especially where there is not at the present time a clinical institute providing for such work in the neighborhood. In connection with this there are several wholesale houses, especially those with a retail branch, who need men qualified to undertake this work.

I have recently visited the laboratory of a pharmacist where, in addition to a very flourishing business as a pharmaceutical chemist, he carries on an extensive bacteriological practice. He conducts urine analyses, both chemical and bacteriological, carries out blood-counts, the examination of secretions for tubercle bacillus, diphtheria, etc., the Wassermann reaction, and the preparation of autogenous and other vaccines. This pharmacist invites and encourages inspection

of his laboratory, and argues that it is better to demonstrate by actual work of this kind than to advocate it by discussions and papers upon the subject. Surely such work can be carried out at other centres by men adequately trained for the purpose.

A pharmacist who is actively engaged in clinical work, and thus closely co-operating with medical men, is obviously bound to attract much of the important work of the preparation and dispensing of drugs. This will tend to relieve the commercial firms of some of the occupations and duties which they frequently assert do not bring a commensurate profit. The exploiting of dispensing at unremunerative rates to act merely as a "bait" for other business is reprehensible and unprofessional. If pharmacy is really to rise, phœnix-like, from the ashes to which it has been reduced, I am convinced it can only be by the evolution of a higher grade of pharmacists who shall be trained to do this kind of work and entitled to practice as clinical analysts and so make pharmacy a more definite professional entity.

PHARMACY IN THE UNITED STATES.

During the war I enjoyed the advantage of spending a year in the United States of America, and visited many pharmacies in different States and cities. It is neither untrue nor unkind to say that in the drug stores there pharmacy is very much more "mixed" than in Great Britain, but occasionally one did meet with firms where little else than dispensing of prescriptions and sale of drugs took place. On the other hand, the schools and colleges of pharmacy are of a very high order, and invariably connected with one of the State universities. The pharmaceutical syllabus consists of a minimum course of instruction of 1200 hours, and in addition to the subjects required for our own examination includes physiology, toxicology, and the action of drugs upon healthy and diseased organs.

It is interesting to note that a Committee of the American Pharmaceutical Association has recently reported upon and outlined a scheme for the institution of two classes of pharmacies—(*a*) drug-stores and (*b*) pharmacies. This scheme is given in detail in the *Pharmaceutical Journal*, May 29, 1920, and well deserves careful consideration. I refer to this, not with a view of suggesting that we should copy their ideas, but to indicate the trend of thought that is taking place in the United States of America. In short, therefore,

practically the whole of the European countries have these higher qualifications of pharmacists, and now America also is seriously discussing this question. Are we to be left hopelessly behind? I am convinced that the time has arrived when we must endeavor to reawaken in the rank and file of pharmacists more of the professional spirit and an outlook beyond the many profit-making schemes that are suggested to us week by week by clever and imaginative advertisers. We must not be content, on the one hand, to benefit by the protection and privileges of a profession, and on the other hand, seriously to compromise the situation by an attitude of complacent commercialism.

THE POLICY FOR THE FUTURE.

In the past we have been far too prone to be the butt of others, and have been content merely to defend our position and our rights. Let us in the future endeavor to use the other means of defense—that is, to attack the positions against us. In the war the immediate objective on most occasions was a short line of trench, some 80 to 100 yards away; but there were always many others beyond, and the final objective was almost present in the minds of those responsible for the "higher strategy." What shall be our "final objective"? Nothing less than the evolution of a real profession of pharmacy. If we do not advance from our present position and secure that these clinical duties shall be performed by pharmacists, there is a grave danger that, with the surplus of medical men and women that will very likely occur in the next few years, we shall find that our objectives have been occupied by others. Besides those holding the medical qualification, there is already an indication that there may be other competitors, for I have recently heard of one school which advertises not only a course for the teaching of dispensing, but, in addition, courses in bacteriological and clinical analyses, which are stated to be framed to fit its students for posts under the Ministry of Health.

In short, my dream is of the institution of a qualification based upon the present Major—and, seeing that the term "Minor" is now obsolete, there is no point in retaining the word "Major"—to be called the Fellowship examination, and that powers should be obtained to entitle the holder to call himself a clinical analyst or clinical pharmacist or registered clinical assistant of the Pharmaceutical Society.

I believe I am right in thinking that some years ago an effort was made by a few prominent pharmaceutical chemists to establish an institute of clinical anlysts, but for various reasons the project fell through. Could not the Society by means of its Major or Fellowship examination, take the place of such an institute, and so render unnecessary the formation of a body outside the Society?

It is repeatedly argued, and with good grounds, that the present Major qualification has little or no pecuniary or other value beyond the confidence which increased knowledge invariably gives; but if the attainment of this examination carried with it the right of registration as a clinical analyst of the Pharmaceuical Society and a Fellowship of the Society, it would immensely increase the value of such a qualification and tend to raise pharmacy in the public estimation.

It is my opinion that a qualification of this kind would attract good men, would be acceptable to the Ministry of Health, would fulfill a need that must arise in the future, and would, by a process of evolution perhaps rather than of differentiation, create a profession of pharmacy which would be collateral, co-existent and interdependent with the medical profession.

EXAMINATIONS REVIEWED.

If it is agreed that we should make this endeavor let us consider the influences we must set on foot to carry out our desires. First there is the question of preliminary general education; but, as I went into this subject pretty fully on a previous occasion and "in another place," I do not intend to say much now. But I should like to repeat that in my opinion it should not be too high a standard to require that every student before registration should pass one of the School Certificate examinations. These examinations have been recognized by the Board of Education as equivalent to and interchangeable with the examination for Matriculation at the Universities and other entrance examinations to professional studies. Apropos of this a very interesting paper was read by Dr. Henry L. Taylor, of Albany, New York, U. S. A., at the Eleventh International Congress of Pharmacy, in September, 1913, at The Hague, entitled "Pharmaceutical Education in Different Countries."

The passing of the Registration examination should, without

doubt, be completed prior to apprenticeship, and it should be a question of honor among pharmacists not to accept an apprentice or pupil until that person has so registered. On my visits to several schools where students have already begun their curriculum of study for Part I of the Qualifying examination I have frequently discovered instances where this point has been overlooked.

Secondly, there is the question of the present Qualifying examination for registration as a chemist and druggist. The division of the Qualifying examination into two parts, and the enforcement of a curriculum of study at approved institutions, is a step the importance of which cannot be over-estimated. I feel sure it will lead before long to a more thorough and permanent education in the sciences which underlie pharmacy, and incidentally to an increased percentage of passes in the examination. I do not advocate, at the present time at least, any serious extension of the syllabus either for Part I or Part II, although some rearrangement of the subjects and readjustment of hours would, in my opinion, be advantageous. I consider there is much to be said in favor of adding to the Qualifying curriculum some outlines of commercial science. If the main work of the chemist and druggist is commercial let that commerce be carried on in a scientific manner, I consider that the syllabus for chemistry, botany, and physics should be one that could be covered by a general elementary course in these subjects as arranged at University colleges and technical schools for students reading for the London Inter-Science examination, First M. B., and others. Personally I should welcome the introduction of written papers, and would be prepared to accept the certificates of certain other examining bodies in lieu of our own Part I—New Syllabus.

The real difficulty is the inability of teachers to deal adequately with the subjects in the time allotted. I am repeatedly told that a whole academic year is required for Part I, especially if the student intends to go on to the Major, or a degree of B. Sc., or the Fellowship of the Institute of Chemistry. Under the present arrangement the teacher finds that "either he has to work to a pattern to make the work of the examiner easy or he is tethered lest he lead his pupil to browse beyond the common plot."

As to the schools for Part II, they will need constant watching and nurturing by the Society, which should look upon them as

branch schools and supply them with diagrams, lantern-slides, and specimens of drugs, so as to humanize and render more practical the courses of instruction in the technical subjects. The teachers of pharmacy in these schools are, for the most part, enthusiastic, capable, and efficient, and endeavor to instil into the students a high ideal of pharmacy as a calling. In many of the schools the students have all the advantages of the corporate life of the college, and the comradeship of students working for the qualifications of other professions. This is in itself a great gain, and one which, indirectly, will do much to increase the prestige of pharmacy in the public estimation. Endeavors should be made to maintain in the mind of the student such ideals that in post-graduate life he may be the better able to take a leading part in the public life of pharmacy and of the country generally. The words of Sir Clifford Allbutt in his Presidential address to the British Medical Association last July can equally be applied to pharmacy. "He (the medical student) may leave his hospital school full of ardor and in rapid growth, but in practice his ardor cools and he drops into routine; or, at any rate, such is his peril, and so less and less may the doctor feel himself a member of a great profession; he may drift out of public affairs, his outlook and sympathies may shrink, his work become a trade, and his medical neighbor his 'opponent.'" It should be the aim of the reorganized local associations to encourage and stimulate among their junior members a continuance of the scientific spirit which they have acquired, at least to some extent at their college or school.

Then, lastly, there is the improved and modified Major examination, which I trust the Council of the Society will proceed with at an early date.

May I offer one suggestion? With a view to creating the qualification of clinical pharmacist it might be advisable to include practical physiological chemistry, and bacteriology (including clinical microscopy) among the compulsory subjects. If certificates of training and examination in these subjects from lecturers and examiners at a medical school similar to those required for the diploma of Public Health were accepted in lieu of the Society's examination in these subjects it would not only make for economy, but the final qualification would carry more weight with the Ministry of Health and medical practitioners.

TO RECAPITULATE.

Pharmacy, if it is to progress, will have to move forward with the advance of general education and of applied science. If it is to take up its position with other professional bodies it must bring its final qualification up to University and Continental standards. If we cannot differentiate between the druggist and the dispensing pharmacist we can at least endeavor to evolve a higher type of pharmacist on the lines suggested.

You will doubtless says that to carry all these things into effect will require an earthquake or a volcano. You will remind me that volcanoes are now extinct in this country, or regulated by formula to erupt only with mild propriety. But, at any rate, they may be considered as some of the "possibilities of the future," and an attempt can be made to bring them nearer to the realm of today. The President of the Society has outlined in his recent memorandum a scheme for organizing its members and associates into properly constituted associations which shall function as local branches of the Society. Two important objects of these local branches are:

(1) To watch the professional interests of pharmacists.

(2) To promote papers upon scientific, technical, and educational subjects.

It is just here, in these local associations, that the professional spirit of pharmacy should be reawakened and discussions encouraged upon various topics initiated by the Society, and possibly assisted by official speakers. To mention a few of these subjects the following might be cited:

(1) Elementary education required for registration.

(2) Conditions of apprenticeship.

(3) The curriculum of study for the Qualifying examination.

(4) The future scope of the Major examination.

(5) The question of granting a Fellowship of the Society to those who proceed to the Major examination.

(6) The work of the Ministry of Health and the duties pharmacists should be called upon to render.

(7) The separation of prescribing from dispensing.

(8) The representation of pharmacists upon the Pharmacopœia Revision Committee.

(9) The disadvantage of encouraging the sale and prescribing of medicines of unknown composition.

(10) The stimulation of practical pharmacists to contribute original work in the compilation of the British Pharmaceutical Codex.

All these subjects are well within the scope of the professional side of pharmacy and discussions upon these matters within local association would doubtless prove of great value. These associations or local branches of the Society could appoint delegates to an annual conference or federation, which would then focus the considered opinion of their members upon professional matters.

Then, again, the various schools of pharmacy would greatly benefit by an interchange of ideas, experience, and methods between the heads of their different departments. An annual conference of such teachers could take place with the object of promoting and advancing the interests of pharmaceutical education.

This brings me to my last point. The British Pharmaceutical Conference has done and is doing a great work in stimulating research and maintaining a high standard of scientific pharmacy. It has for over fifty years annually brought together pharmacists and others interested in pharmacy from all parts of the United Kingdom and Ireland and oft-times has welcomed those from the overseas Dominions. It has published a "Year-Book of Pharmacy," of which it may well be proud. It has received year by year the hearty welcome and enjoyed the unstinted hospitality of the local Committee, and especially of the municipal authorities of the cities at which its annual meetings have been held. It has been a reunion of those who for the most part have been imbued with a true professional spirit. It has received delegates from local associations, and has frequently discussed educational problems. Cannot the Conference absorb within its constitution and administration the suggested Federation of Local Associations and the Association of Pharmaceutical Teachers? Has the Conference the necessary authority and funds?

During the war the paramount necessity for unity of control was seen to be vital if victory was ultimately to be achieved. In British pharmacy today there is need for a closer union of "purpose, counsel and activity" of all those who are working for a full realization of the profession of pharmacy.

One of my dreams is of a central unifying association which shall bring together and co-ordinate those forces of which I have been speaking. The union of these forces—education, qualification, research, and professional conduct—should result in the evolution of a real profession of pharmacy, which, co-existent and inter-dependent with medicine. should work for the advancement of the health of the great nation to which we belong. Some of you may say:

"I talk of dreams,
Which are the children of an idle brain,
Begot of nothing but vain fantasy."

May I not claim, at least?

"I had a dream, which was not all a dream."

THE THEORIES OF BLOOD COAGULATION.[1]

By Jules Bordet,

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First of all, I beg of you to excuse my imperfect knowledge of the English language and to accept my best thanks for the honor you have conferred upon me by inviting me to deliver the Herter lectures. I shall try today to give a brief *résumé* of the chief theories which have been held concerning the mechanism underlying the coagulation of the blood. This phenomenon deserves our interest not only because of its physiological importance but also as a striking example of the resources of experimental analysis. It can occur *in vitro,* and this is a very favorable condition for the success of investigation. Nevertheless, and although it has been the subject of innumerable researches, up to the present time, its mystery has not been completely disclosed. You will not expect me to attempt a detailed review of the whole subject. I shall give only such broad outlines as will serve to make clear the

[1] Lecture I of the Herter Series, delivered before the Johns Hopkins University on Tuesday, October 26, 1920.—From the *Bulletin of the Johns Hopkins Hospital.*

modern conceptions which seem to afford the best explanation of this complicated process, and which, therefore, especially deserve our attention.

It is hardly necessary to remind you that coagulation is nothing else than the aggregation, into meshes of fibrin, of particles of fibrinogen, a substance which, as Fredericq showed 43 years ago, pre-exists as a dispersed colloid in the circulating plasma. When the blood flows from a wound, the first determining factor which, through successive modifications of the plasma, assures the solidification of fibrinogen, is not infrequently the mixture of the blood with very active principles liberated by the bruised tissues, or in other words, the addition to the blood of tissue extract. But such an influence is an additional one, foreign to the blood itself; hence, limiting the problem, I shall consider here, exclusively, the coagulation that the blood is capable of showing, solely by means of its own substances.

A most important, even a decisive factor of this automatic coagulation, is the contact of a foreign solid body (glass, for instance), which acts only physically by its presence, since it does not liberate any soluble substance. The contact, external factor, brings into activity the internal factor, belonging to the blood, and that is the process through which the principle directly and immediately responsible for the coagulation, the fibrin-ferment or thrombin, is produced. In fact, the thrombin, which is found in large quantities in the clot or in the serum, does not exist (as Schmidt showed many years ago), in the circulating blood. Consequently, several stages are to be distinguished in the total process, the most important one being the period in which the thrombin appears, the fibrinogen itself playing merely a passive rôle. Fibrinogen can be extracted by special methods and obtained in a fairly pure condition, but it must be kept in mind that the essential problem presented to the physiologist is the coagulation, not of pure fibrinogen, but of the blood considered as a whole, that is, of a very complex medium, cellular and plasmatic, having a definite reaction and definite osmotic pressure, containing numerous constituents, and especially colloids, which presumably are apt to influence each other through molecular adhesion. Coagulation could not be studied without taking into consideration every influence apt to interfere in the phenomenon.

Since the blood of mammals, as a rule, clots promptly, it seemed

essential to the success of the investigation to determine how the course of the process could be protracted and, moreover, how it could be stopped at the first period of its evolution, so as to make possible the separation of the cells from the still liquid plasma. Several methods have been devised; I shall mention them very briefly.

Concentrated salts, magnesium sulphate for instance, hinder the coagulation. Common salt especially answers the purpose, being a normal constituent of the organism. Blood from the artery to which from three to five per cent. of salt has immediately been added yields by centrifugalization a clear plasma which does not clot so long as the high saline concentration is maintained, but which, when diluted with an amount of distilled water sufficient to re-establish the normal saline content, clots rather quickly. Decalcifying salts, the type of which is sodium oxalate, prevent completely the coagulation, calcium salts being necessary to this phenomenon. By centrifugalization a clear plasma is obtained, which tends to clot when a soluble calcium salt, such as calcium chloride, is restored.

Coagulation is also prevented if to the active contact of glass a contact is substituted, which is not, if we may so express it, felt by the blood or the plasma. A liquid does not feel a wall, I mean does not react physically to it, unless it is capable of adhering to it. Freund was the first to show that blood flowing from the artery does not clot, or at least clots very slowly, when received in a vessel the inside of which has been coated with oil or vaseline. Since it forms a solid coating, paraffin is very suitable to such experiments, and frequently permits the separation of the cells and the plasma by centrifugalization. In conjunction with Gengou I observed that by these means a clear plasma can be obtained and be kept fluid for twenty-four hours, but that clotting soon occurs when the plasma is brought into contact with glass. This experiment shows that the contact of glass can bring about its effect without the presence of any cells, that is, without any vital interference—we have to do with a physico-chemical phenomenon.

The blood of certain animals, namely, birds and fishes, as Delezenne has shown, clots very slowly by itself, coagulation being greatly hastened by the addition even of traces of tissue extract. Without the help of decalcification or of paraffin coating the blood of a bird will remain fluid for a long time and even yield by centrifugalization a permanently liquid plasma, provided that the tube in-

serted into the vessel has not been allowed to touch the wound, and consequently no trace of tissue extract has become mixed with the blood. As a matter of fact, this precaution ought to be taken regularly, whatever may be the species of animal under experiment, as it is quite a general rule that tissue extract accelerates coagulation, this auxiliary influence being particularly noted for birds, because this blood is not so capable of spontaneous coagulation as is that of mammals.

Thanks to such methods, the separation of the two constituents, cells and plasma, can be attained before any beginning of coagulation and—let us emphatically insist upon this essential fact—before any appearance of the coagulating principle, thrombin. There is no need to remind you that serum yielded by coagulation contains thrombin.

We must now try to go further and subject plasma and cells to a closer analysis. Let us consider first the plasma. Soluble calcium salts are necessary to coagulation. How do they act? Pekelharing and Hammarsten have shown the essential fact that these salts are not necessary to the transformation of fibrinogen into fibrin under the influence of thrombin, but are indispensable to the formation of the latter, that is, to the production of thrombin from the mother-substances already present in the circulating blood. The production of thrombin is prevented by oxalate, but on the other hand decalcification does not prevent the coagulation of the fibrinogen by completed thrombin. Indeed, it has been proved that blood, oxalated immediately after withdrawal from the artery, remains permanently fluid, no thrombin being ever detected in it, whereas if serum yielded by normally clotted blood be oxalated, this oxalated serum, added to oxalated plasma, causes the coagulation of the latter. From these facts it follows that oxalated plasma is a most suitable reagent for the detection of thrombin in a given liquid; indeed, an estimation of the coagulating power of such a liquid may be made by taking into consideration the quantity of oxalated plasma coagulated by a certain amount of this liquid, or the rapidity of the occurring coagulation. But it must be borne in mind that, at least when present in serum, the activity of a given thrombin depends not only upon its quantity but also upon its age. The capacity of fresh serum to coagulate oxalated plasma decreases very quickly, by a spontaneous attenuation of the thrombin, and this

fact affords a possibility of detecting whether a given thrombin has been produced quite recently or some time ago. Several experiments, as we shall see, require such a determination.

Contact is also necessary to coagulation. How does it operate? I showed with Gengou, many years ago, that contact is in a way analogous to calcium, or in other words, that contact with a foreign solid body (paraffin of course excepted) is necessary to the appearance of thrombin, but is not requisite for the coagulating influence of the latter. When blood is received into a paraffined vessel, thrombin is not formed; when received into a glass vessel, thrombin is produced in the zone of contact, a fact which explains why coagulation begins along the wall. But when serum yielded by previously clotted plasma is added to blood or plasma kept in a paraffined vessel, the entire mass rapidly solidifies the paraffin no longer exerting any inhibiting influence. This experiment explains why blood freshly drawn and placed in a glass vessel coagulates in a mass much more rapidly when shaken.

What then is the origin of thrombin? It does not exist as such in the circulating blood, although the latter contains everything requisite for its production. The circulating blood, therefore, contains the mother-substance, or mother-substances, of thrombin, which, for convenience, may be called prothrombin, and which in the early stages of coagulation is converted into thrombin. What is prothrombin?

Sixteen years ago Morawitz made an important discovery in this connection. He found that if crushed tissue, muscle for example, is added to serum yielded by normal coagulation, the coagulating power of this serum towards oxalated plasma is considerably increased. And yet, the extract of tissue by itself does not contain any thrombin, since without the help of serum, it is incapable of coagulating oxalated plasma. Hence, we are forced to conclude that the tissue extract contains something which is not thrombin, but which reacts with the serum so as to produce this active principle. Thence follows at once the hypothesis that thrombin is derived from the interaction of two different substances, the one furnished by the tissue cells, the other by the serum. Undoubtedly, even before the introduction of the tissue extract, a certain amount of thrombin existed in the serum, but it seems as if this fluid contained also an excess of the mother-substance, the latter being capable of reacting

with the tissue extract so as to generate a fresh supply of thrombin.

But the question immediately arises whether such an assumption, deduced from experiments in which tissue extract plays an important rôle, may be without further question applied to the automatic coagulation of pure blood. As a matter of fact, it must be kept in mind that injected into the circulation, the tissue extracts are highly toxic, causing sudden death due to intravascular coagulation. Undoubtedly they contain some coagulating principle foreign to the blood itself. This substance upon which I shall not dwell today, our present task being merely the study of the coagulation of pure blood, in all probability, is of an albuminoid nature, and is markedly thermolabile. It is specifically related to the tissues, does not exist in the blood, and could not be considered as a real mother-substance of thrombin. But we must immediately add that, besides this peculiar principle, the tissue cells, nevertheless, contain one of the two mother-substances of thrombin. This exists also in the blood cells, is of lipoid nature and may be designated *cytozyme*. The other mother-substance, called by us *serozyme*, is furnished by the blood fluid and is present in the serum. But let us see how these determinations have been arrived at?

The assumption that the blood cells furnish one of the mother-substances of thrombin is in perfect accordance with the results of experiments dealing with the part played by those cells, and chiefly by platelets, in the coagulation. Platelets can be easily separated by centrifugalizing oxalated blood at a moderate speed for a short while; being very light, they remain in suspension, whereas red and white corpuscles are thrown down, the turbid supernatant fluid pipetted off being very rich in platelets. Now if such a platelet-plasma is centrifugalized for a long time and at a very nigh speed, the platelets finally are sedimented and a clear plasma may be obtained from which the platelets have not been thoroughly eliminated, this being impossible, but in which they are present only in small numbers. Comparing these two plasmas, the one very rich, the other very poor in platelets, Lesourd and Pagniez found that after recalcification the former clots rapidly, the latter slowly. Completing these experiments, with Delange, by comparing the coagulating influence, on oxalated plasma, of the two serums yielded respectively by the coagulation of plasma rich in platelets and of plasma poor in plate-

lets, we observed that the former serum contains a much larger quantity of thrombin than the latter. Consequently, the platelets actively participate in the production of the coagulating principle. This fact can be proved more distinctly by the following experiment: A sediment constituted exclusively of these small cells is obtained by vigorously centrifugalizing oxalated plasma, previously freed of its red and white corpuscles, but containing still its platelets. This platelet deposit, thoroughly washed, is emulsified in physiological solution, and one drop of the turbid emulsion thus obtained is added to a certain quantity of a serum which, being derived from the slow coagulation of recalcified oxalated plasma that has been freed of its own platelets, is by itself very poor in thrombin. Within 20 or 30 seconds, the mixture becomes capable of coagulating a suitable amount of oxalated plasma almost instantaneously; in other words the reaction of serum with platelets generates an abundant supply of thrombin. It must be pointed out that this experiment closely resembles that of Morawitz except that platelets instead of tissue cells are added to the serum. Tissue cells and platelets both contain one of the generators of thrombin, which may be called *cytozyme*. The second one, the *serozyme*, exists in the serum. It can be easily demonstrated that the reaction between serum and platelets, that is to say, between serozyme and cytozyme, takes place only in the presence of soluble calcium salts, no thrombin appearing if the serum has been decalcified before the introduction of the platelets. Moreover, I shall further insist on the fact that the two substances unite, that they really consummate each other. Indeed, experience shows that when a serum has been treated once with platelets, and has yielded thrombin, this serum is subsequently incapable of reacting with a new amount of platelets, its serozyme having been exhausted by the first reaction. It follows that a serum produced by the coagulation of a plasma rich in platelets and which of course contains much thrombin, is considerably less rich in serozyme, that is, considerably less capable of reacting with new platelets, than is a serum derived from a plasma deprived of most of its platelets. This is precisely what experience shows. It is, therefore, highly advisable always to employ for serozyme a serum obtained by the coagulation of oxalated plasma which has been carefully freed of its platelets before recalcification.

Serozyme is a thermolabile substance, easily destroyed by heat.

No thrombin is produced when platelets are added to serum that has been exposed to a temperature of about 56° C. On the contrary, cytozyme, the active principle of platelets, may be heated to a hundred degrees and even higher without losing its properties; cytozyme is thermostable and, furthermore, can be easily extracted.

A thick emulsion of platelets, treated with a large excess of absolute alcohol, gives an extract from which, by evaporation a residue is obtained which is soluble in alcohol, ether, toluol and chloroform but insoluble in acetone, thus exhibiting the characteristics of lipoids, and especially of lecithin. This residue acts as a very powerful cytozyme.

As we were able to show eight years ago traces of this lipoid behave exactly as do platelets, generating thrombin when added to serum, hastening the coagulation of recalcified oxalated plasma or causing the coagulation of spontaneously non-coagulable bird's plasma. The same lipoid, possessing exactly the same properties may be extracted from tissues, from muscle for example. Cytozyme is thus a lipoid.

These facts having been obtained about cytozyme, what is serozyme? Serozyme is certainly furnished by the plasma, not by the cells. Platelets contain cytozyme; they yield thrombin when mixed with serum but they are never able to liberate thrombin when kept in physiological solution or in distilled water, even in the presence of calcium salts. They consequently contain only one of the mother-substances, not both of them. The liability of serozyme towards heat allows us to presume that this substance is of an albuminous nature. Its fragility would be a very serious hindrance to its isolation, but for one of its properties—a really fortunate one. The serozyme shows a strong tendency to adhere to mineral precipitates, barium sulphate or calcium fluoride for example. This is the reason why, as I discovered many years ago with Gengou, those precipitates, added to oxalated plasma wholly suppress in the latter the property of coagulating by subsequent recalcification; one of the mother-substances, the serozyme, which is absolutely requisite for the production of thrombin and consequently for coagulation, has been entirely removed. I have found more recently, in conjunction with Delange, that tricalcic phosphate is especially powerful as an absorbent. When diluted in physiological solution, this substance gives a rather gelatinous emulsion, a very slight quantity of which,

added to blood flowing from the artery, prevents its coagulation. By centrifugalization and pipetting off, a clear plasma is obtained, which remains fluid, even when platelet emulsion, or tissue extract, or lipoidic cytozyme, is added. This is easily understood; both mother-substances, serozyme and cytozyme, are equally necessary to the production of thrombin; it is of no use to add one of them if the other is absent. But such a plasma, which we may for the sake of brevity call "phosphate plasma," clots under the influence of thrombin or, which naturally is the same, when both mother-substances are added. It behaves as an excellent reagent for the detection of thrombin. Since its composition closely resembles that of the original plasma, it may be considered as being fibrinogen dissolved in a normal medium.

But tricalcic phosphate is endowed with a property which is remarkably useful for technical purposes. As is well known, it is capable of being dissolved in physiological solution under the influence of a current of carbonic oxide gas. Consequently, phosphate which has been added to plasma and has absorbed the serozyme, after having been thoroughly washed, can liberate, thanks to its own dissolution, the active principle it had withdrawn. In this way, Delange and myself succeeded in bringing about the isolation of serozyme, which, on the addition of cytozyme extracted from platelets, gave abundant thrombin. Thus in the course of the whole experiment the factors which determine coagulation are in reality subjected to an analysis followed by a synthesis.

As mentioned above, our assumption that serozyme and cytozyme are the generators of thrombin involves the idea that those mother-substances really unite to form a compound, which is thrombin. This ought to be demonstrated also with regard to pure cytozyme, I mean a cytozyme in the condition of a lipoidic extracted matter. If the union really occurs, we may anticipate that, if a given quantity of serozyme be mixed with a sufficient amount of cytozyme, thrombin will be engendered and the serozyme will be exhausted; in other words, it will be no longer capable of yielding fresh thrombin when a new amount of cytozyme is added. Such is indeed the case. Serum yielded by coagulation of recalcified platelet-free oxalated plasma is divided into two parts, lipoidic cytozyme being added to one of them, the other portion being kept as it is. In the tube containing both serum and cytozyme, thrombin

appears, the activity of which is very strong at the outset, but decreases as we know, very rapidly, so as to become quite attenuated by the following day. On the next day, lipoidic cytozyme, and, several minutes afterwards, oxalated plasma are added to both tubes. Then the tube which has received cytozyme on the preceding day does not clot at all, or does so only very slowly, whereas the tube, to which cytozyme has just been added for the first time, clots almost instantaneously.

It is clear that such an experiment makes it possible to ascertain whether the same cytozyme, endowed with the same binding properties as the pure lipoid, exists in fresh or heated platelets, or in tissue juice, ground muscle for example. Adequate experiments show that serum which has already reacted with any one of such materials does not generate any more thrombin when subsequently brought into contact with any one of them. For example, serum to which lipoidic cytozyme has been added will not react any more either with the same lipoid, with platelets, or with muscle juice, and conversely.

Without entering into details, I may add that the manner in which the two substances unite closely resembles the mode of union of toxins and antitoxins, in that the process is not governed by the law of strict and constant equivalents, but takes place in varying proportions, thus seeming to result not from true chemical affinities but from contact affinity or molecular adhesion. But another fact, more noteworthy for its bearing upon the underlying mechanism of coagulation is disclosed by the determination of the lapse of time required for the union of both substances.

Serozyme being found in serum may be assumed to exist also in the oxalated plasma from which this serum has been derived. Now if cytozyme and serum are mixed, thrombin appears very quickly; it is only a question of some seconds. But—and this fact is undoubtedly remarkable—if cytozyme be added, not to serum yielded by coagulation of recalcified oxalated plasma, but to an identical oxalated plasma recalcified just before, that is, at a moment when this plasma is still perfectly fluid, the appearance of thrombin is greatly delayed. In other words, serozyme reacts with cytozyme quickly when present in serum, slowly when present in plasma. We thus reach the conclusion that the serozyme does not exist in the same condition in plasma as in serum, that in plasma it is not

capable of reacting at once with cytozyme. We may express this fact by saying that plasma contains proserozyme instead of active serozyme, one of the first phenomena of the whole process of coagulation being precisely the conversion of proserozyme, unfit until transformed to unite with cytozyme, into serozyme capable of this reaction.

The notion that in original plasma or in circulating blood, serozyme does not exist as such, that is, does not exhibit affinities toward cytozyme, satisfactorily explains why intravascular injections of the latter substance are, as we found, quite harmless. But the blood of such injected animals shows, when shed within about half an hour after the injection, a strikingly increased tendency to rapid coagulation. This fact as we have pointed out may probably be available for therapeutic purposes in cases of hemorrhage.

Is it now possible to investigate under what influences the proserozyme is converted into serozyme, in other words, under what influences does it acquire the capacity of reacting with cytozyme?

To solve this problem, we have at our disposal a very adequate technic, based on the use of oxalated salt-saturated plasma.

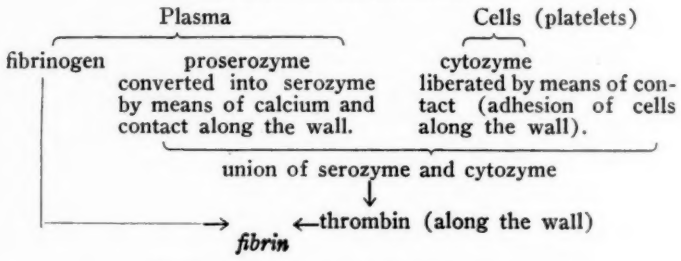
Some minutes ago I mentioned the fact that when oxalated plasma is saturated with common salt, the fibrinogen is entirely precipitated. After strong centrifugalization, pipetting off and elimination of the excess of salt by dialysis in presence of physiological oxalated solution, the supernatant fluid represents exactly normal oxalated plasma, except that, having lost all of its fibrinogen, it cannot coagulate. Being oxalated it does not contain any trace of thrombin, but is still capable of producing plenty of it on the addition of calcium salt and cytozyme. Now if a calcium salt and cytozyme are added thrombin appears indeed, but only after a rather important delay. Half an hour, and sometimes more, must elapse before the mixture becomes capable of bringing about an almost instantaneous coagulation of a fibrinogen solution. Thus the acquisition of the ability to react with cytozyme, that is, the conversion of proserozyme into serozyme, requires a notable length of time. Now, on the other hand, if the aforesaid fluid without fibrinogen is recalcified and cytozyme is added one or two hours later the thrombin appears almost instantaneously. This experiment clearly illustrates the essential assumption that the whole process of the production of thrombin, the first stage included, which is the conversion of pro-

serozyme into serozyme henceforth capable of uniting with cytozyme, takes its course without any participation of fibrinogen.

Furthermore, the conversion of proserozyme, which as we know cannot take place without calcium salts, is—and the fact is noteworthy—strikingly favored by contact with glass. The capacity of reacting with cytozyme appears only after a much longer lapse of time when the recalcified fluid is kept in a vessel coated with paraffin. Consequently, the influence of contact, which is so obvious in coagulation, is not exerted through some interference of fibrinogen, but really acts without any help of the latter, as a factor of thrombin production. It is highly probable that contact by way of absorption, frees the liquid of some antagonistic substance, most likely some protective colloid, which prevented the serozyme from reacting with cytozyme, that is, maintained it in the inactve condition of proserozyme. On the other hand, experiments show that the presence of cytozyme likewise facilitates such a liberation of serozyme, owing to its strong affinities towards the latter principle.

To sum up, we are now able to follow the schema which indicates the order of succession of the phenomena.

SCHEMA OF COAGULATION


Plasma
Cells (platelets)
fibrinogen
proserozyme converted into serozyme by means of calcium and contact along the wall.
cytozyme liberated by means of contact (adhesion of cells along the wall).
union of serozyme and cytozyme
thrombin (along the wall)
fibrin

(contact and calcium no longer necessary)

I think that the schema symbolizes quite accurately the most prominent features of the whole process and distinctly shows the sequence of events. But the mechanism underlying coagulation as it occurs under ordinary conditions is still somewhat more complicated, owing to a peculiar property of thrombin. Thrombin results from the union of serozyme and cytozyme, but these two substances combine in variable proportions. The consequence is that a given complex, when rich in serozyme, is able to capture an additional amount of cytozyme, and, when rich in cytozyme, which

is ordinarily the case in the coagulation of whole blood, shows a marked affinity towards a new amount of serozyme. As a matter of fact, such an affinity is so strong that it causes thrombin to attract and to possess itself of serozyme even when this principle is still present in a state of proserozyme. Consequently, finished thrombin acts as though it could bring about a remarkably quick conversion of proserozyme into serozyme, the process preliminary to the genesis of fresh thrombin being thus greatly hastened. The consequence is that, when thrombin is added to oxalated plasma which has been just recalcified, the total amount of thrombin this quantity of plasma is apt to furnish appears much more rapidly than it does when the same plasma is allowed to clot spontaneously without the stimulus of thrombin. In fact, thrombin itself thus accelerates the formation of thrombin. Owing to lack of time, I cannot report here in detail the experiments which have established this idea, but shall now consider briefly some of the views held by certain authors and which are not in agreement with the ideas developed above.

As is well known, my countryman, the physiologist Nolf, has adopted the rather startling theory of Wooldridge according to which, instead of being the immediate determining factor of coagulation, thrombin is generated as a consequence of the coagulation itself. According to Nolf, the transformation of fibrinogen into fibrin is not the effect, but the necessary condition of the appearance of thrombin. Many of the data which I have recorded above energetically plead against such a conception. For example, I would only recall the experiments showing the production of thrombin in fluids altogether devoid of fibrinogen, and thus proving unquestionably that fibrinogen does not play any rôle in the production of the coagulating principle.

One important point has been and still is controverted. I mean the true significance of the lipoid to which we have so often alluded. Schmidt, who had already observed the accelerating influence on coagulation, exerted by alcoholic extracts of tissues, believed that such lipoids rendered easier the production of thrombin, without assuming, as I do, that they really enter into its constitution. One of the most distinguished among the writers who have devoted their skill to the study of coagulation, Professor Howell, especially directed his attention towards the fact that the lipoid extracted, for example, from nervous tissue, is capable of

inducing the coagulation of peptone plasma and hirudin plasma which, as is well known, remain fluid because they contain an anti-coagulating substance, called antithrombin. In opposition to our assumption, Howell thinks that the lipoid is not a constituent of thrombin, but acts by neutralizing the antithrombin, which hindered the spontaneous conversion of prothrombin into thrombin. The real existence of antithrombin is of course unquestionable and it has been proved beyond doubt that antithrombin may be neutralized by thrombin, the two substances being, in all probability, capable of forming a compound. Now the question arises whether, when lipoid is added to peptone or hirudin plasma, the removal of the antithrombin function is due, as Howell claims, to the direct neutralization of antithrombin by this lipoid, or to a neutralization of antithrombin by thrombin generated under the influence of the same lipoid, the latter reacting with the serozyme or proserozyme also contained in the aforesaid plasma. In other words, according to this second interpretation, the neutralization of antithrombin by the lipoid would be merely apparent or at least indirect, the direct agent of this neutralization being the thrombin which the lipoid has caused to appear. I believe that such a conclusion is forced upon us by some recent and careful experiments by Gratia. Without entering into the somewhat complicated details, they have shown that the lipoid does not at all neutralize the antithrombin when the serozyme or proserozyme has been previously removed, that is, when the production of thrombin has been made impossible. Even when the lipoid is added in large excess, the abolition of the antithrombin function occurs only in proportion to the amount of serozyme present, that is, in proportion merely to the quantity of thrombin that can be generated. Consequently, a direct influence of the lipoid on the antithrombin cannot be admitted.

Furthermore, Howell's view could hardly be brought into harmony with a very essential fact, which has been mentioned above. Were his assumption correct, it should be admitted that serum yielded by the coagulation of recalcified oxalated plasma deprived of its platelets contains a large amount of antithrombin, since the addition of lipoid to such a serum, itself poor in thrombin, produces in this fluid plenty of the latter principle; upon the whole, the serum should in this respect resemble very closely the plasma from which it is derived. But, such being the case, it would be very difficult to

understand why the lipoid neutralizes the antithrombin very quickly when added to serum, and very slowly when added to plasma. I think the only possible explanation of such a difference is that in serum but not in plasma, as was said before, the serozyme is capable of reacting very rapidly with cytozyme to generate thrombin. However, the question as to the relation of cytozyme to the antagonistic function is one of the most delicate in the whole study of coagulation and I fully realize that different views may still be upheld. As I told you at the beginning, coagulation has been studied for years and years by many investigators; none of them can presume that the problem is yet solved; every one of them merely indulges in the hope of gathering some complementary data; a little more information.

ATROPINE SULPHATE FROM DATURA STRAMONIUM.*

By H. W. Rhodehamel
and E. H. Stuart.

An interesting and valuable lot of data concerning the preparation of atropine from Datura Stramonium, commonly known as Jimson weed, is presented by the authors.

The percentage of total alkaloids in the plant is said to vary from 0.15 to 0.6 per cent. The seeds contain the highest amount, next come the leaves, and the lowest amounts are found in the stems, particularly in the woody portions, where the figure runs below 0.10 per cent.

The method of extraction was by the use of 0.2 per cent. aqueous solution of sulphuric acid preserved with 0.5 per cent. of formaldehyde.

The dilute solution of atropine sulphate was treated with Lloyd's reagent, which consists of a hydrated siliceous (Fuller's) earth.

Different fractions of the percolate were treated with appropriate amounts of Lloyd's reagent, after which the reagent was allowed to settle, the exhausted percolate was decanted and the precipitate drained and thoroughly dried at a temperature of about 50° C.

The percentage of alkaloidal material recovered from different

*Abstract of a publication from the Research Department of Eli Lilly & Co., Indianapolis, Ind.

lots ranged from 33.98% to 93.06%, the larger amounts being recovered when larger proportions (359 pounds to 5000 gallons, representing 15,500 pounds green Stramonium) of the reagent was added.

The adsorbed alkaloids were recovered by extraction with ether after making alkaline.

The reagent, after extraction, always contained about 0.2 per cent. of alkaloid, which could not be economically removed.

Experiments in which other acids were used to facilitate extraction showed no marked differences from those recorded, although other preservatives, such as bleaching powder, cresol, and sodium bisulphite, gave better results than formaldehyde in the matter of the yield of alkaloid.

The crude alkaloidal material recovered from the "reagent" was purified as follows:

PURIFICATION OF THE CRUDE ATROPINE.

The alkaloidal material was extracted from the Lloyd's reagent with 95 per cent. alcohol, using lime to obtain the proper alkalinity. The extractions were acidulated with acetic acid and the solution concentrated first to 12 per cent., and then under diminished pressure to 2 per cent. of its original volume. This procedure was sufficient to convert all the hyoscyamine into atropine. After neutralization with ammonia, the solution was allowed to stand over night and filtered. A test portion of the filtrate was shaken with ether. If an emulsion resulted, the solution was diluted about one-fourth and returned to the vacuum still. Distilling the neutral liquid, and again filtering, usually prevented the troublesome emulsion with ether. Ammonia was added until the solution was alkaline and the atropine alkaloid extracted with ether. After evaporation of the ether, the alkaloid was carefully dried at about 35° C.

The dried alkaloid was dissolved in ethyl alcohol in the proportion of one ounce of alkaloid to two fluid ounces of solvent, and the solution almost neutralized with sulphuric acid, using cochineal as indicator. After filtering it was evaporated on the water bath to a thin sirup, and to this sirup, while still warm, acetone was added almost to the point of precipitation of the atropine sulphate.

On cooling, the atropine sulphate crystallized. If not sufficiently

pure the crystals were dissolved in alcohol and recrystallized as outlined above.

The acetone was evaporated from the mother liquor, and the alcoholic solution of atropine sulphate poured into a large volume of water. From this the alkaloid was extracted with ether, and if not of sufficient purity the process already outlined was repeated.

DRUG RESEARCH.*

Declaring that all humanity would be benefited by the establishment of a $10,000,000 national institute of drug research in the country, Edwin E. Slosson, editor of the *Science Service* of the National Research Council, in a recent address before the American Drug Manufacturers' Association in Washington, D. C., stated that the making of drugs was developing along the lines of discovery and cultivation of new medicinal plants and in the invention of synthetic remedies. He said in part:

"The day of the shotgun dose has gone by. The modern doctor uses a rifle. In former times it often happened that the antiseptic aimed at a bacillus and killed a phagocyte. Before the era of recent research the best of antiseptics was carbolic acid. Yet carbolic acid applied to a wound killed off the invaders and defenders of the bodily citadel with almost equal impartiality. This is as if the United States entering a war in defence of France, had showered poison gas all along the front and wiped out both the German and French armies.

"The Bible recommends us to beat our swords into plowshares, but the chemist has gone farther in turning a poison gas into a perfume. The war delivered into our hands a chemical industry for which we were not fully prepared and by which we have not fully profited. We are now producing more tons of dyestuffs than we formerly imported, but some of the most important dyes are not yet made in America. In the field of pharmaceutical research I am told that we are not even keeping up with the procession, to say nothing of leading it. The plan proposed by the American Chemical Society for a national institute of drug research with an endowment of $10,000,000 ought to be carried out, for it would benefit not only our own country but all humanity.

*Through the *Canadian Pharm. Journ.*

"In the drug business there is opportunity for development in all three of these lines. First, in the discovery of new medicinal plants; second, in their cultivation for the increase of the active principle; and third, for the invention of synthetic remedies. A pharmaceutical survey should be made of the tropical territory under the control of the United States and whenever any plant is found which may reasonably be suspected of concealing anything of value about its person it should be taken into custody and placed in a reformatory where its principle might be strengthened.

"The misnamed vitamines are now being separated and concentrated and may eventually be produced as pure chemical compounds which may be administered in a pill to correct a deficiency of diet. Possibly they may be made synthetically and even now vitamines are invented that will stimulate the growth of a particular organ or regulate some specific bodily process. But we shall not have to resort to vitamine pills if we plan our diet properly.

"Here is the borderland where foods and drugs come together, and I venture to predict that the distinction between them will ultimately be wiped out. I believe that the doctors will become dietitians and drug-manufacturers will devote themselves largely to the preparation of regulated foods. Bran biscuits may well serve as substitutes for Epsom salts and air-dried spinach for iron citrate. In other words, I look for the merging of medicine into hygiene. There will be less need for remedies when more attention is paid to preventives."

OIL OF CADE.*

By C. T. BENNETT, B. Sc., F. I. C., F. C. S.
Pharmaceutical Chemist.

"Huile de Cade" has always been somewhat variable in character, particularly as regards specific gravity. According to the British Pharmacopœia, the specific gravity is "about 0.990," but during the last few years there has been some difficulty in obtaining an oil with a specific gravity over 0.975. A good deal of this oil is now distilled in Spain, from which country some 50 tons are exported annually. According to Ménasché (*Perf. and Ess. Oil Record*, 1921, p. 149), the specific gravity of the genuine Spanish

*From the *Pharm. Journ. and Pharm.*, August, 1921.

oil may be as low as 0.955. The limits given in the United States Pharmacopœia are 0.980 to 1.055 at 25°, and up to the last few years most commercial samples have fallen within these limits. It seems, however, that the minimum figure will have to be lowered. Possibly the variation is due to the method of distillation and the amount of tar present in the oil.

Genuine cade oil must be derived exclusively from the wood of *Juniperus oxycedrus* by dry distillation. *Juniperus oxycedrus* is a bushy shrub, differing from the other Juniper species by the simultaneous occurrence of needle-shaped leaves and of fruits which are orange-red when ripe. It grows on a chalky marly soil, and thrives best in a southern aspect. It occurs abundantly in the wild state in Provence and in the waste lands of Sommeres and Lussan. The woodcutters distinguish two kinds of wood, "cades gras" and "cades maigres"; only the former is used for distillation, the latter serving as fuel. The heart-wood is richest in oil, and the oil-content is said to increase towards the roots. For the purpose of distillation the bark is removed and the wood is then cut as small as possible. The preparation of the wood is very important, as the yield of oil is much greater from shavings than from larger chips. The distillation is carried on throughout the year, but preferably from September to May.

According to Pépin ("Recherches sur l'Huile de Cade Vraie," Paris, 1908) the oil is obtained by two methods in France—"distillatio per descensum" and by "combustion en milieu confiné." The former method is used only in the manufacture on a small scale. A cast-iron boiler is filled with shavings, then turned upside down on to its cover or a hollowed-out stone slab, and cemented up. In the centre of the bottom is a hole, which is connected with a delivery tube. A brisk fire is lighted so that the boiler is surrounded by the flames. Distillation commences with evolution of thick vapors, and soon afterwards a blackish viscid liquid flows off. The process lasts from half an hour to several hours, according to the quantity of wood. In place of a boiler a pit is sometimes used, with a stone slab at the bottom provided with a delivery pipe. The chips are heaped up in the centre of the cavity and covered over with bricks, which are luted together with clay. The rest of the pit is used for firing material.

The second process, that of incomplete combustion with exclusion of air, is used for production on a large scale. For this purpose a brick kiln is employed, 18 feet to 22 feet long and about 6 feet high, with an inclined bottom provided with a gutter, which allows the oil to drain into a vessel placed in a pit in front of the exit. The kiln is covered with earth except at the place where the cavity is, and for the purpose of filling it up with wood and setting fire to the latter, large openings are provided at the top and sides. After the fire is lighted these openings are closed, and distillation proceeds with simultaneous carbonization of the wood. The distillation frequently lasts several days. When the fire is too hot the resulting oil is more viscid and blacker than under normal conditions when the color is reddish-brown. The fresh distillate is left standing for two or three weeks, when it separates into three layers, of which the upper one is the oil of cade, the next is water, and the lowest consists of tarry products. Such methods of preparation must necessarily lead to variation in the characer of the product.

According to Pépin, the specific gravity lies a little below 1.000; it makes a clear solution with 8 to 10 volumes of 96 per cent. alcohol, and in all proportions with ether, amyl alcohol, chloroform, acetic acid and benzene. The water-soluble acid-content should not exceed 1.5 per cent. calculated as acetic acid. When distilled at ordinary atmospheric pressure the fraction boiling between 150° and 300° should amount to 68 to 80 per cent., whilst pine tar yields only 15 per cent. between these temperatures. For the detection of pine tar oil the best test is the copper acetate reaction. One cc. of the oil is shaken with 15 cc. of petroleum ether and the mixture is then filtered. To 10 cc. of the filtrate an equal volume of a 5 per cent. solution of copper acetate is added and well shaken, 5 cc. of the petroleum ether layer is diluted with 10 cc. of ether and filtered. In the presence of pine tar oil the filtrate has an intense green color, whilst pure cade oil gives a chestnut-brown color.

Cade oil of Spanish origin, though of low specfic gravity, contains a high proportion of cadinene, as shown by fractionation, and does not give a reaction for pine tar. It is guaranteed to be derived from *Juniperus oxycedrus,* and may, therefore, be accepted as genuine cade oil. The extreme limits for specific gravity I have observed for this oil during the last twenty years are 0.955 and 1.064.

VITAMINES AND THEIR DISTRIBUTION.*

Two years ago a report was published by a committee appointed jointly by the Lister Institute and the Medical Research Committee, detailing briefly "The Present State of Knowledge Concerning Accessory Food Factors (Vitamines)." The findings of this committee are of great interest. At the end of the report a valuable table is given, showing the distribution of the three vitamines in the commoner foodstuffs. In the absence of quantitative data it was impossible for the committee to do more than indicate the relative values of the foodstuffs as sources of the various vitamines, by the rough method of positive and negatives signs. The table, with slight modifications, follows:

Classes of Foodstuff.	*Fat-Soluble A or Anti-rachitic Factor.*	*Water-Soluble B or Antineuritic (Antiberi-beri) Factor.*	*Antiscor-butic Factor.*
Fats and Oils:			
Butter	+ + +		
Cream	+ +		
Cod-liver oil	+ + +		
Mutton fat	+ +		
Beef fat or suet	+ +		
Peanut oil	+		
Fish oil, whale oil, etc.	+ +		
Margarin prepared from animal fat	Value in proportion to amount of animal fat contained		
Nut butters	+		
Meat, Fish, etc.:			
Lean meat (beef, mutton, etc.)	+	+	+
Liver	+ +	+ +	+
Kidneys	+ +	+	
Heart	+ +	+	
Brain	+	+ +	
Sweetbreads	+	+ +	
Fish, white		very slight, if any	
Fish, fat (salmon, herring, etc.)	+ +	very slight, if any	
Fish, roe	+	+ +	
Canned meats	?	very slight	

*From the *Journ.* of the *A. M. A.* August, 1921.

Classes of Foodstuff.	*Fat-Soluble A or Anti-rachitic Factor.*	*Water-Soluble B or Antineuritic (Antiberi-beri) Factor.*	*Antiscor-butic Factor.*
Milk, Cheese, etc.:			
Milk, cow's whole, raw	+ +	+	+
Milk, skim, raw	.....	+	+
Milk, dried, whole	less than + +	+	less than +
Milk, boiled, whole	undetermined	+	less than +
Milk, condensed, sweetened	+	+	less than +
Cheese, whole milk	+		
Eggs:			
Fresh	+ +	+ + +	?
Dried	+ +	+ + +	?
Cereals, Pulses, etc.:			
Wheat, maize, rice, whole grain.	+	+	
Wheat germ	+ +	+ + +	
Wheat, maize, bran	.....	+ +	
Linseed, millet	+ +	+ +	
Dried peas, lentils, etc.	.....	+ +	
Soy beans, haricot beans	+	+ +	
Germinated pulses or cereals ...	+	+ +	+ +
Vegetables and Fruits:			
Cabbage, fresh (raw)	+ +	+	+ + +
Cabbage, fresh (cooked)	.....	+	+
Cabbage, dried	+	+	very slight
Cabbage, canned	.....	.....	very slight
Swede (rutabaga) raw expressed juice	.....	.....	+ + +
Lettuce	+ +	+	
Spinach (dried)	+ +	+	
Carrots, fresh, raw	+	+	+
Carrots, dried	very slight		
Beetroot, raw, expressed juice..	.....	.....	less than +
Potatoes, raw	+	+	
Potatoes, cooked	.....	.....	+
Beans, fresh, scarlet runners, raw	.....	.....	+ +
Onions cooked	.....	.....	+ at least
Lemon juice, fresh	.....	.....	+ + +
Lemon juice, preserved	.....	.....	+ +
Lime juice, fresh	.....	.....	+ +
Lime juice, preserved	.....	.....	very slight
Orange juice fresh	.....	.....	+ + +
Raspberries	.....	.....	+ +
Apples	.....	.....	+
Bananas	+	+	very slight
Tomatoes (canned)	.....	.....	+ +
Nuts	+	+ +	

Classes of Foodstuff.	Fat-Soluble A or Anti-rachitic Factor.	Water-Soluble B or Antineuritic (Antiberi-beri) Factor.	Antiscor-butic Factor.
Miscellaneous:			
Yeast, dried	.....	+ + +	
Yeast extract and autolized	?	+ + +	
Malt extract	.....	+ in some specimens	

None of the three factors were found in:
Lard.
Olive, cottonseed, coconut or linseed oils.
Coco butter.
Hardened fats, animal or vegetable in origin.
Margarin from vegetable fats or lard.
Cheese from skim milk.
Polished rice, white wheaten flour, pure cornflour, etc.
Custard powders, egg substitutes, prepared from cereal products.
Peaflour (kilned).
Meat extract.
Beer.

THE CULTIVATION OF ERGOT.*

Whether ergot can be successfully cultivated on a large scale is a question that has of late often been asked. The drug was formerly collected chiefly in Russia and Galicia; smaller quantities came from Spain and Algeria, but very little from Central and Western Europe. The present scarcity is due to the absence of supplies from Russia and Galicia, and as these countries will probably not export any for a considerable time, the conditions are favorable for the attempt at cultivation on a scale sufficiently large to allow of export.

The investigations of Tulasne and Kühn have made us familiar with the life-history of ergot. The sclerotium is developed in the summer in the inflorescence of certain Graminaceous plants and replaces the ovary; when mature it falls to the ground, retaining its vitality until the following spring. Numbers of stromata with their characteristic spherical heads then develop from the sclerotium. In

*Abstracted from "Die Kultur des Mutterkornes," by Prof. L. Hecke, Vienna (*Schweiz. Apoth. Ztg.*, 59, p. 277). Reprinted from *Pharm. Journ. and Pharm.*

warm weather the stromata ripen quicky, the color passing from yellow to violet; in them myriads of perithecia are formed, and in these the asci containing the very slender spores are developed. These spores are ejaculated from the perithecia, and, being carried by the gentlest currents in the atmosphere, are raised in the air and borne to the flowers, which must be open to receive them. A single spore entering an open flower and resting on the ovary is sufficient to cause the infection. The spore develops, the ovary perishes, and its place is taken by a whitish, cheesy mass of mycelium which, in about eight days, forms multitudes of conidia and simultaneously secretes a viscous, sweet honey-dew, the "sphacelia segetum" of the older authorities. This is visited by various insects (*Melanostoma mellina, Rhagonycha fulva, Sciara Thomæ,* etc.), and the honey-dew, with the conidia suspended in it, is carried to other plants where further infection is effected, provided, of course, that open flowers are still present. The sphacelia gradually hardens to a sclerotium, on the apex of which its remains are often to be found in the form of a whitish cap (still containing conidia).

Ergot occurs not only on rye, but also, though less frequently, on barley, rarely on wheat, but often on a large number of wild grasses, *e. g., Anthoxanthum, Arrhenatarum, Dactylis, Festuca, Phalaris, Briza, Calamagrosti,* etc. On other grasses special forms may occur which will not develop on rye; for example, a form is found on *Lolium perenne,* which will not develop on rye, but which can pass to *Bromus, Molinia,* and other grasses.

Rye is the only host practically available for the cultivation of ergot, but it is hopeless to expect success from sowing ergots in a rye field. This has been tried and has failed. Infection depends on so many circumstances that the quantity of ergot produced may easily be less than the quantity sown. In the most favorable instances barely one per cent. of the grain harvested will be ergot. The infection must be artificial. The sclerotium is necessarily the starting-point, and it must be induced to germinate at the right time, for if the discharge of the spores does not coincide with the flowering of the rye no infection can take place. The conditions of germination must therefore be accurately known. Ergots will not germinate satisfactorily unless they have wintered in the open; if kept in a room and then sown in the spring they will germinate either badly or not at all. Probably the frost has some action on the sclerotium

as it has in the case of the teleutospores of certain russ. A rest period appears to be necessary, but its length is unknown.

As far as is at present known, ergots are best germinated by sowing them about one centimeter deep in boxes of sandy earth in the autumn, and then sinking the boxes in the open ground. They will then germinate with perfect regularity in the spring, when the weather is warm and moist. If necessary the boxes may be covered with glass. Sclerotia that have been made capable of germination by exposure to frost can be taken up in February and kept dry till wanted. Rapidity of germination appears to depend chiefly on the temperature; at ordinary room temperature the first stromata will appear in about a fortnight. The ejaculation of the spores can easily be observed under a strong lens; it lasts at least several days, and is influenced by warmth and moisture; it may even cease and then recommence. Although the number of spores ejaculated from each head is very large, their direct utilization for the purpose of infection is not feasible. The spacelia with its condia is much better adapted for this purpose. Large quantities can be produced either on the rye grain itself or by means of a pure culture. In the former case several inflorescences are enclosed in glass tubes closed at each end with cotton, wool, and ergots with ripe asci are introduced. As the flowers open they become infected and produce honey-dew in about eight days; this can be collected, suspended in water, and the suspension used in a spray for infection on a large scale. This method is attended by numerous practical difficulties, and it is preferable to obtain the quantity of sphacelia necessary by pure culture. This is easily done by allowing the spores to be ejaculated from the perithecia on to nutrient gelatin in Petri dishes. The spores germinate at once, and the colonies can be transferred, together with a small piece of the gelatin, to a suitable nutrient medium contained in large flasks. In these enormous quantities of conidia are produced. Further propagation by inoculation is easy, so that there is no difficulty in having the necessary amount always at hand. As the sclerotia can be induced to germinate during the winter the cultivation of the sphacelia can be carried on during the spring at a time convenient for the flowering of the rye. The cultures are shaken with water, and the suspension used with a spray.

Infection is very difficult. It can be accomplished only when

the flower is open, and is, therefore, practically confined to such flowers as open and are subject to cross-fertilization. Barley and wheat are seldom attacked, as they are self-fertilized, and the flowers do not open. Rye is usually cross-fertilized, the self-fertilized flowers being sterile; the flowers open when the anthers are ripe. The time during which the flower remains open depends on the time at which fertilization is effected, and varies. Isolated rye plants by the wayside or scattered in fields of wheat where the prospects of fertilization are small may keep their flowers open for a week, and these are the plants that are most commonly infected by ergot. In the case of fields of rye in which clouds of pollen are produced fertilization is quickly effected and the flowers close. The flowering of a field of rye is over in about a week; this is about the time the sphacelia takes to develop after the spore has attacked the ovary. The conidia produced by the sphacelia, therefore, finds no flowers open and ready for infection, and this method of the further dissemination of the ergot is not available. In the cultivation of ergot the endeavor must accordingly be made to hinder the fertilization as much as possible, and so prolong the period of flowering. With this object in view, the rye should not be sown in fields, but in single rows between rows of other plants, such as maize. Damp, windless weather is unfavorable for fertilization, and, therefore, favorable for the dissemination of the ergot. Sites for the cultivation of ergot should be sought in damp localities where the air is still.

Another method of prolonging the time during which the open flowers are available is by sowing at intervals of a week or fortnight. The plants should be about ten centimeters aparts, so as to favor the development of several stems with inflorescences developing at different times. Special species or varieties, such as *secale montanum,* may also be sown. By such means the duration of the flowering may be extended from the middle of June to the end of September.

The cultivator visits the plants daily, or more than once a day, and sprays the open flowers with conidia suspension. Once infection is effected, further dissemination is carried out by natural means. There is no doubt that the cultivation on a large scale is feasible, but it must be carried out by specially trained workers. The danger of infecting rye fields in the neighborhood of the cultivation is

small, and a distance of 100 meters would probably be sufficient to ensure safety, particularly if the cultivation is carried out with late-flowering species.

Experiments are now in progress with the view of ascertaining whether the cultivation is likely to be financially successful.

SCIENTIFIC AND TECHNICAL ABSTRACTS

HYDROGEN PEROXIDE; DETECTION AND DETERMINATION OF TRACES OF ——. F. W. Horst. *Chem.-Zeit.*, 1921, 45, 572.—Traces of hydrogen peroxide may be determined qualitatively and quantitatively by reduction with ferrous sulphate, and colorimetric estimation of the ferric sulphate formed by means of ammonium thiocyanate. The ferrous sulphate solution must be freed from traces of ferric salt by passing hydrogen sulphide through it, first in the cold and then at the boiling point, and is cooled in a current of carbon dioxide, Twenty cc. of the sample to be tested is placed in a graduated tube, and a few cc. of petroleum spirit is added as a protection against oxidation during the reaction. About 2 cc. of the ferrous sulphate solution is added and agitated with the sample by means of a current of carbon dioxide. Five cc. of air-free ammonium thiocyanate solution is then introduced, and the color is compared with that of a standard solution.—W. J. W., through *Journ. of Soc. of Chem. Ind.*

AMMONIUM SULPHATE AS A WEED KILLER.—Reporting on sulphate of ammonia as a weed-killer, the Experimental Station of the Rhode Island State College says that this method of reducing or eliminating weeds from lawns was developed there by a series of experiments extending over twenty years. All lawn grasses require in order to grow at their best that the soil be supplied with plenty of plant food in the three elements found in commercial fertilizers—nitrogen, phosphorus and potassium. Most grasses and weeds also require that the soil be not sour; but some kinds which make an even turf grow well in an acid soil. The usual fertilizers employed

for top-dressing lawns in the spring do not develop acidity, and permit the coarsely growing weeds to crowd out the grass. Nitrogen is commonly furnished in nitrate of soda, which tends towards an alkaline reaction. By substituting a similar amount of sulphate of ammonia, which is not more expensive, an acid condition of the soil is gradually produced which weakens the weeds, while not affecting the special grasses referred to—bent Grasses or Fescues. Thus in two or three seasons the weeds will entirely disappear, or in new lawns will never become troublesome. The phosphorus can be applied in acid phosphate, and the potash in muriate of potash, as usual. Different soils require different amounts of plant food; but a good proportion for average conditions is 250 pounds of sulphate of ammonia, 400 pounds of acid phosphate, and 250 pounds of muriate of potash to the acre. A smaller quantity than this should be used on newly-seeded lawns. A too heavy application of sulphate of ammonia will injure the grass as well as the weeds; but in the proportion noted it may safely be used as freely as the common lawn fertilizers. It is necessary that the fertilizer be distributed evenly when the lawn is dry, in order not to burn the grass; and where convenient it is well to sprinkle the lawn thoroughly after applying the fertilizer.—*Gas Journal,* through *Chem. Trade Journ.,* July 30, 1921, 128.

An Ideal Zinc Ointment.—Mr. A. H. Clark, of the School of Pharmacy, University of Illinois, read a paper before the American Pharmaceutical Association on the best formula for zinc ointment from the standpoints of therapeutic activity and keeping qualities. He found that an ointment made with lard produces a disagreeable odor and becomes granular. With lanoline and yellow soft paraffin an unpleasant odor develops. White wax gives an ointment that is very liable to shrink. The ideal ointment is obtained with the following formula:

Soft white paraffin	65 parts
Hard paraffin	15 parts
Zinc oxide	20 parts

This ointment is odorless, does not shrink, nor does it separate or granulate.

OIL OF WILD PIMENTO LEAVES.—According to Roberts ("J. S. C. I.," 1921, 40, 94) the essential oil distilled from the leaves of *Amomis jamaicensis* contains 17 per cent. of terpenes, including dipentene and α-phellandrene, 15 per cent. of eucalyptol, traces of aldehydes, 38.3 per cent. of alcohols, principally *l*-linalol with some geraniol, 1.5 per cent. of linalyl acetate, and traces of phenols and free acids. Sesquiterpenes are also probably present.—Through the *Chem. & Druggist.*

ESSENTIAL OIL OF JUNIPERUS TAXIFOLIA.—Shinosaki (*Journ. Chem. Ind., Japan,* 1921, 24, 202) has obtained 0.24 per cent. of a pale green oil by distillation of the leaves and twigs of *Juniperus taxifolia,* a coniferous plant growing in the Ogasawara Islands. The oil contains about 50 per cent. of α-pinene, in both the dextrorotatory and the lævorotatory varieties. A second terpene, apparently bicyclic, is present, a free alcohol of the formula $C_{10}H_{18}O$, an ester, a sesquiterpene, and a sesquiterpene alcohol.—Through the *Chem. & Druggist.*

SIAM BENZOIN.—Reinitzer (*Arch. Pharm.,* 1921, 259-60) publishes further details of his investigation of the constituents of Siam benzoin. Lubanol benzoate $C_{17}H_{16}O_4$ crystallizes in plates melting at 72°-73°. It becomes oxidized by exposure to the air, and then exhibits the series of color changes which are identical with those shown by the crude gum resin itself. On heating, it evolves benzoic acid, and then gives off an odor of carnations, and eventually of guaiacol. It is believed that lubanol is either identical with, or closely related to, coniferyl alcohol. This point can only be decided when pure lubanol itself is obtained in the crystalline condition.—Through the *Chem. & Druggist.*

OIL OF ERGOT.—A freshly-gathered sample of ergot from Obersteiermark yielded only 21 per cent. of oil on extraction with petroleum ether, the saponification value of which was 196.2, as compared with the only previously recorded figure of 180. The neutralization value of the insoluble fatty acids, 194.8, and the acetyl saponification value, 248.7, were similar to those of a sample that had been kept for ten years. The acetyl value, 86.6, was, however, higher in

the case of the fresh oil. The melting point of the fatty acids was 39.5° C., and the solidifying-point 38.6°-36.5° C. by the capillary method.—K. Gander and J. Zellner (*Seife*, 1921, 6, 411, through *Journ. Soc. Chem. Ind.*, July 30, 1921, 518A).

MANUFACTURE OF LUMINOUS PAINTS.—Four methods for the manufacture of phosphorescent pigments are described. The first utilizes oyster shells as the raw material. The shells are first washed with hot water and then dried and calcined at a bright red heat. After cooling, the mass is crushed and freed from the *débris* of the external layers, which is valueless for the purpose in hand. The shell powder is then mixed with a small amount of powdered wood charcoal and transferred to a crucible made of a refractory earth, where it is arranged in alternate layers with powdered sulphur. The crucible, covered by a lid securely luted on, is strongly heated for about an hour, and after complete cooling the mass is extracted and pulverized once again. A phosphorescent color prepared in this way from an impure carbonate of lime possesses a more intense lustre than the colors made from pure carbonate of lime. In the second method the sulphates of calcium, barium, or strontium are used as the raw materials. These are intimately mixed with powdered wood charcoal, in the proportions of 1 part of carbon to 5 or 6 parts of sulphate. The mixture is then calcined as in the previous process. In the third method, when working with carbonates such as marble, witherite, or carbonate of strontium it is necessary to add, in addition to the wood charcoal, rather more than one chemical equivalent of sulphur, and then to proceed in the same manner as with the oyster shells. The second and third processes give masses with an orange, green, blue or red phosphorescence. The sulphur is sometimes replaced by antimony sulphide or other similar sulphur compounds. More luminous but more expensive colors can be produced by starting with calcium oxide, barium carbonate, or carbonate or sulphate of strontium, either alone or mixed with calcium oxide or marble. The necessary carbon is obtained from starch, which is mixed with the above substances. The carbonates of rubidium and lithium, as well as bismuth nitrate, are equally of service. Sometimes sodium sulphate, or even lead acetate, is added, and the formulæ for the mixings vary with each individual factory. It may be

taken as a general rule, however, that about 80 parts of the principal constituent require 12 parts of sulphur (or less if other sulphur compounds be present); 4 to 5 parts of starch, 2 to 4 parts of lithium carbonate, and 0.01 to 0.5 part of other metallic compounds. Those constituents, which are used only in very small amounts, are best added in alcoholic solution. The mixtures are heated in a hermetically sealed crucible for three-quarters to one hour at a temperature of about 1200° C. Phosphorescent pigments are, when used, often mixed with barium sulphate, lakes of natural coloring matters, and often with mineral pigments of the same shade as the prosphorescent body itself. Thus, for example, realgar is used with red shades and orpiment with yellow shades.—O. Prager (*Chem. Tech. Fabrikant,* through *Chem. Trade Journ.*, August 6, 1921, 158).

Alkaloids of Valerian.—Goris and Vischniac (*Répert. de Pharm.*, June 6, 1921) extracted 5 kilos. of an aqueous extract of valerian, representing 40 kilos. of fresh root, with a 10 per cent. solution of sodium carbonate, treating the liquid with a mixture of ether and chloroform, then with water containing 2 per cent. of hydrochloric acid, finally saturating this solution with carbonate of potassium, and successively extracting with ether and with chloroform. They succeeded in obtaining 4 gm. of crude bases, from which they were able to separate 3 gm. of chantinine and 1 gm. of valerine. The former is difficult to obtain in a crystalline form, except as the picrate, which melts at 97° to 98°. Animal experiments showed that these two alkaloids have practically no physiological action; the therapeutic properties of valerian are therefore not due to these two bodies.—Through the *Chemist & Druggist.*

Saccharin Reaction.—L. Thevenon, a pharmacist in Oullins, describes a new reaction of saccharin (*Jour. Pharm. Chim.*, No. 11, 1920). On adding 10 cc. of a solution of 0.1 gram of sodium nitrite in 100 cc. of distilled water, and six drops of sulphuric acid (1/3), to a solution containing 0.1 gram of saccharin in 25 cc. of distilled water, the further addition of 0.1 gram of beta-naphthol to the mixture causes the immediate production of an intense red coloration, which may be fixed to wool and silk, and is permanent.

It is sufficiently sensitive to detect traces of saccharin in foodstuffs, after extraction by alcohol and water in the usual way, preferably adding the sulphuric acid to the solvent employed for extraction.—Through the *Chemist & Druggist.*

A New Method for the Estimation of Morphine.—Trifon Ugarte (*Journ. de Pharm. et de Chim.,* February 16, 1921). One gram of powdered opium is introduced into a flask of 200 cc. capacity, and 10 cc. of alcohol (67 per cent.) is added. The mixture is placed on the water bath for five minutes, and then filtered. The filtrate is collected in a crystallizing pan with a diameter of 7 centimetres and 2 centimetres deep. The insoluble portion is treated successively three times as described, and the filtrates collected in the crystallizing pan. The collected liquids are evaporated on the water bath, and the dry residue is maintained for 15 minutes at a temperature of 100°, to oxidize the resins, and thereby render them insoluble; 5 cc. of cold distilled water is now added to the residue and filtered into a flask having a capacity of 200 cc. This operation is repeated three times, and the collected 20 cc. of liquid is evaporated on the water bath. The residue is dissolved in 2 cc. of water saturated with morphine, and under agitation 3 cc. of normal solution of ammonia saturated with morphine are added, as well as 10 cc. of ether, and the whole shaken. The shaking causes a rapid fall in temperature, due to the evaporation of the ether. A further addition of 20 cc. of ether is made, and the mixture set aside for 30 minutes. The morphine now crystallizes out in the form of small granules. After adding 10 cc. of ether the mixture is filtered, the crystals of morphine are removed by means of a glass rod provided with an India rubber cap, and by the use of a jet of distilled water saturated with morphine and ether. The filters are then dried at a temperature of 100° to 105° and weighed.—Through the *Chemist & Druggist.*

The Effect of Alkalinity on the Use of Hypochlorites.—E. K. Rideal and W. R. Evans, in the *Journal of the Society of Chemical Industry,* point out that the keeping qualities of solutions of hypochlorites are enhanced by the presence of free alkali, but that when used as disinfectants or for treatment of water to destroy

organisms, they act more efficiently when acid; in fact, the oxidizing power of these solutions is greatly depressed by the presence of alkali. They suggest for treatment of alkaline waters the simultaneous addition of nitre cake.

The variability of chlorinated lime—as it reaches the consumer—appears to have considerable public importance. One sample (packed in paper) purchased at a local store was found to contain only traces of available chlorine. The unstable character of chlorinated lime—even at low temperatures—is little appreciated. It decomposes very rapidly if exposed to damp air or to carbon dioxide. Solution of sodium hypochlorite keeps much more satisfactorily, so long as it is kept in a cool place, protected from light and from access to carbon dioxide.—J. S. C. I., Feb. 28, 1921.—Through the *Aust. Journ. of Pharm.*

Approximate Estimation of Commercial Cresol in Lysol. C. J. Jordan and F. Southerden. (*Pharm. J.*, 1921, 106, 479-480.)—Products of somewhat varied composition are sold under the name "lysol," but most of them consist essentially of a strong solution of castor oil or linseed oil soap incorporated with commercial cresol. To estimate the amount of cresol present 60 gm. of the sample is acidified with 30 cc. of dilute sulphuric acid and steam-distilled until the distillate no longer gives a blue coloration with ferric chloride. The whole distillate is shaken thoroughly, but not too violently, so as to ensure saturation of the aqueous layer, and then set aside for a few hours. The volume of the cresol layer multiplied by 1.04 and added to one-fiftieth of the volume of the aqueous layer gives the weight of cresol in the portion of the sample taken. The method yielded trustworthy results in the case of mixtures containing known amounts of cresol. It is generally agreed that "lysol" should contain 50 per cent. of cresol, but analyses of ten different brands showed that in some cases the cresol content was about 40 per cent., and in one sample 35 per cent.—W. P. S., through *The Analyst*, Sept., 1921.

Mitragynine and Mitraversine, Two New Alkaloids From Species of Mitragyne. E. Field. Chem. Soc. Trans., 1921, 119, 887-891.—The residue obtained by evaporating the alcoholic ex-

tract of the leaves of *Mitragyne speciosa* (N. O. *Rubiaceæ*) when dissolved in glacial acetic acid, freed from chlorophyll and resin by addition of water, and made alkaline with ammonia, yields an amorphous precipitate, which when dissolved in 20% acetic acid and treated with a hot aqueous solution of picric acid yields a crude picrate, $C_{22}H_{31}O_5N.C_6H_3O_7N_8$, orange-red needles from methyl alcohol, m.p. 223°—224° C., representing 0.3% of the initial weight of the leaves. The free alkaloid is obtained by dissolving the picrate in boiling glacial acetic acid and pouring into dilute ammonia, filtering while hot. The new alkaloid, for whch the name mitragynine is suggested, is a colorless amorphous solid, m. p. 102°—106° C., distilling unchanged at 230°—240° (5 mm.); it contains three methoxy groups, but no N-methyl groups, and is probably $C_{17}H_{22}N(OCH_3)(CO_2CH_3)_2$. Hydrolysis with sodium ethoxide gives a dicarboxylic acid, m.p. 280°. Both this acid and alkaloid give the indole reaction with hydrochloric acid and vanillin. The acetate, mono- and trichloro-acetates, and the hydrochloride are described. Similar treatment of the leaves of *M. diversifolia* gives an alkaloid, for which the name mitraversine is suggested, having m. p. 237° C. molecular weight 328, and containing 2 methoxy groups. The hydrochloride melts at 208°—210°. It is probably $C_{22}H_{26}O_4N_2$.—P. V. M., through *Journ. of Soc. of Chem. Ind*

NEWS ITEMS AND PERSONAL NOTES

FREE PUBLIC LECTURE COURSE, 1921-1922, PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE, 145 NORTH TENTH STREET.

First Lecture. Thursday evening, October 6, 1921. "The Chemistry of Other Worlds." By Prof. Henry Leffmann, A. M., M. D., Lecturer on Research, Philadelphia College of Pharmacy and Science; Hon. Prof. Organic Chemistry, Wagner Free Institute of Science, etc.

Modern astronomy, especially by the aid of photography, has enabled us to obtain much information about the physical and chemical nature of the heavenly bodies. In addition to the members of our own system—sun, moon and planets—immense numbers of fixed stars exist, which with comets, nebulæ and meteors, have furnished

additional facts. It appears that the forms and compositions of all these bodies are much like those of our own planet, but peculiar conditions are occasionally found. One remarkable incident was the finding of an element in the sun before it was known to exist on the earth, and the subsequent discovery of it in certain parts of the United States in amounts sufficient to make it available for war purposes. This lecture will present, vividly, by lantern slides, many interesting facts concerning the form and nature of the heavenly bodies, and incidentally discuss the possibility of the existence of intelligent beings on other worlds.

Second Lecture. Thursday evening, October 20, 1921. "Petroleum and Its Products and Their Modern Uses." By Prof. F. P. Stroup, Ph. M., Professor of Chemistry, Philadelphia College of Pharmacy and Science.

A brief resume of the occurrence, methods of production and refining of petroleum, and a discussion of the properties and uses of its products, with special reference to motor fuels. Illustrated with lantern slides and specimens and a working model of oil well machinery.

Third Lecture. Thursday evening, November 10, 1921. "Products From Cotton Fields and Forests." By Prof. J. W. Sturmer, Phar. D., Professor of Pharmaceutical Chemistry, Lecturer on Industrial Chemistry, Philadelphia College of Pharmacy and Science."

The industries based upon the chemical utilization of cellulose, the substance which constitutes cotton fiber and which may be separated also from wood pulp, are of increasing importance. Varnishes, artificial leather, artificial silk, celluloid, paper of all description and kinds, paper clothes, and scores of other products, are manufactured in great quantities. The lecture, which will be illustrated, will deal with the newer aspects of this subject.

Fourth Lecture, Thursday evening, November 17, 1921. "Strawberries at the North Pole and Apples at the Equator." By Prof. Heber W. Youngken, A. M., Ph. D., Professor of Botany and Pharmacognosy, Philadelphia College of Pharmacy and Science.

An exposition of the recent methods of dehydration as employed for the preservation of foods of various classes. The ad-

vantages of these methods over desiccation, evaporation, cold storage, heat and chemical processes. This lecture will be illustrated with a variety of dehydrated products.

Fifth Lecture. Thursday evening, December 15, 1921. "Our Bacterial Friends and Enemies (The One Class to Be Protected and the Other Destroyed)." By Prof. Louis Gershenfeld, B. Sc., Professor of Bacteriology, Philadelphia College of Pharmacy and Science.

The micro-organisms—their discovery and classification. Development and scope of bacteriology. The general characteristics and activities of bacteria. Their relation to health and disease. Bacteria in humans and animals, air and soil, drinks and foodstuffs. Bacteria of value and harmful in the arts and industries.

Sixth Lecture. Thursday evening, January 5, 1922. "Chemistry in Peace and War." By Prof. P. Fischelis, B. Sc., Phar. D., Consulting Chemist, Member Editorial Staff, *The Journal of Industrial and Engineering Chemistry;* Dean of the New Jersey College of Pharmacy.

The dependence of America in peace-time pursuits and the possibility of transforming these industries, when necessary into factories for producing engines of destruction, poisonous gases and high explosives.

Seventh Lecture. Thursday evening, January 19, 1922. "A Thousand and One Odors" (Of interest to those who use perfumery and those who desire to make it). By Prof. E. F. Cook, Ph. M., Director of the Pharmaceutical Laboratory, Philadelphia College of Pharmacy and Science.

First Part. A popular presentation of the history of perfumery with a description and samples of those materials from material sources which the perfumer can utilize and a brief, illustrated story of their production and marketable forms.

Second Part. An account of the synthetic production of perfumes, their chemical character and a display of samples of the artificially produced flower odors.

Third Part. A display of modern perfumes and perfumed products.

Eighth Lecture. Thursday evening, February 2, 1922. "Standardized Remedies" (How they conserve life and what the public should know about them, including the newer serums and vaccines). By Prof. Paul S. Pittenger, B. Sc., Lecturer on Physiological Assaying, Philadelphia College of Pharmacy and Science.

How drugs are tested for strength and value by modern scientific methods, including a brief description of some of the newer biological remedies, such as serums, vaccines, etc.

Ninth Lecture. Thursday evening, February 16, 1922. "How Chemistry Develops the Industries" (Of particular appeal to men and women who wish to apply chemistry in manufacturing). By Prof. Frank X. Moerk, Ph. M., Director of the Chemical Laboratory, Philadelphia College of Pharmacy and Science.

Examination of raw materials and final products; increased production; utilization of waste products. Rapid methods of examination.

Tenth Lecture. Thursday evening, March 2, 1922. "One Drop of Blood" (The story of health and sickness told in a most fascinating way). By Ivor Griffith, P. D., Ph. M., Serologist and Clinical Chemist, Stetson Hospital, Philadelphia, Editor *American Journal of Pharmacy;* Instructor in Pharmacy, Philadelphia College of Pharmacy and Science.

Its constituents, its role in health and sickness. The mechanism of coagulation. Its changes in disease. Its constant defensive warfare. Invasion of bacterial hordes. The summoning of the great white hosts, their mode and instruments of warfare, the hidden hormones, the unknown enzymes, and the subtle platelets. The bacteria are overcome and cannibalized and the disease conquered, the day is won and life persists.

Eleventh Lecture. Thursday evening, March 16, 1922. "The Foods of the Next Century." By Prof. Chas. H. LaWall, Ph. M., Sc. D., Chemist to Food Bureau, Pennsylvania Department of Agriculture; Professor of Pharmacy, Philadelphia College of Pharmacy and Science.

A brief historical survey of foods with particular reference to new and interesting foods of the present and the probable development of the future in this interesting and important field.

Twelfth Lecture. Thursday evening, April 5, 1922. "The Raw Materials of the Chemical Industry." By Prof. Samuel P. Sadtler, Professor Emeritus of Chemisty, Philadelphia College of Pharmacy and Science.

The successful development and establishment of a chemical industry is primarily based upon a supply of cheap and satisfactory raw materials.

For the inorganic chemical industries these are:

Fuels, including coal, petroleum oil and natural gas; salt, either solid or in the form of brine, limestone; sulphur or pyrites; phosphates; nitrates.

For organic industries:

Fuel, as before stated; wood and cellulose fibre; other textile fibres; sugar and starch yielding raw materials.

Review of the position of the United States in respect to these materials.

Thirteenth Lecture. Thursday evening, April 29, 1922. "Food From the Air." By Dr. Henry Leffmann, A. M., M. D.

A popular and interesting account of how the nitrogen of the air can be made to enter into such combinations as make it available for many industrial and commercial processes. The newer work on the up-building of proteins makes it possible to expect a food supply from the air at some not far distant date.

Fourteenth Lecture. Thursday evening, May 4, 1922. "Natural Silk and Artificial Silk." By Dr. Chas. E. Vanderkleed, Lecturer on Chemical Control, Philadelphia College of Pharmacy and Science; During the World War With Hercules Powder Company.

Comparisons and contrasts between natural silk and artificial silk. Methods of preparation of natural silk and of manufacture of artificial silk. Commercial uses and possibilities of both varieties.

DR. JOSEPH JACOBS, OF ATLANTA, GEORGIA, IS HONORED BY THE UNIVERSITY OF GEORGIA.—A recent issue of the *Atlanta Georgian* carries the following report of honors bestowed upon Dr. Jacobs, a

loyal member of the Philadelphia College of Pharmacy and Science, and an earnest worker in the ranks of pharmacy:

"Thousands of Georgians will heartily indorse the action of the University of Georgia in bestowing the honorary degree of doctor of science on Dr. Joseph Jacobs, a loyal alumnus of the university and scholar who has conferred distinction on his Alma Mater by his distinguished achievements in science during his professional career.

"Doctor Jacobs, who was a member of the Class of 1879 and was a pupil of Dr. Crawford W. Long, has devoted many years to the development in pharmaceutical use of plants indigenous to the South and it was because of the importance of that work, as well as his literary work and research in establishing beyond a doubt the priority of Dr. Crawford Long's discovery of ether-anesthesia that he was given the honorary degree.

"One of the features of the commencement season at Athens this year was the unveiling of the medallion in memory of Dr. Crawford W. Long, presented by Doctor Jacobs.

"Doctor Jacobs also authorized the trustees of the university to offer in his name $50 in gold as an annual prize for the best paper submitted by a student on Doctor Long and his discovery of anæsthesia.

"After the unveiling of the medallion to Doctor Long, the three daughters of the great discoverer presented to Doctor Jacobs an oil painting of their father.

"In presenting the monument and medallion to the university, Dr. Jacobs made an address in which he spoke of his association with Dr. Long, and extolled the value to humanity of the discovery of ether anæsthesia.

> "'That I have been permitted to present this monument to the University of Georgia, and that her trustees have accorded me the honor of its acceptance,' declared Dr. Jacobs, 'fills my heart with sentiments of gratitude and pride.
>
> "'My early boyhood and all my adolescent years were spent in this good city of Athens, and of her I can truly say:
>
> "'"Where e'er I've roamed, what other realms to see
> My heart untraveled, has fondly turned to thee."
>
> "'It was during those years of my life in Athens that Dr. Crawford W. Long, whose wonderful achievement we here commemorate, was my employer in pharmacy and my much respected tutor. The countless acts of friending by which he then benefited me, I have, in all the years, treasured in recollection with "miser care." And hence, in considering how I might in appropriate form attest some small measure of my apprecia-

tion of the man and his invaluable contribution to the welfare of humanity, I thought these shades in which he pursued his academic studies, here, at his alma mater—old Franklin College—the proper place for a record of its expression.

" 'Dr. Crawford W. Long was a graduate of this university of the Class of 1835. Although he completed a full medical course at the University of Pennsylvania, and benefited by practical experience in the hospitals of New York City, yet I have often thought that, from the spirit of the motto of our university, the spirit of research, *"et docere, et causas rerum exquirere,"* "both to teach and to seek out the causes of things," he formed the habit of clear and patient observation of facts, which enabled him, in the exercise of his deeply humane and sympathetic nature, to make his unexcelled discovery, in the realms of the curative science, for which he will be known in all future time as the conqueror of surgical agony. The day, March 30, 1842, on which Dr. Crawford W. Long discovered ether anæsthesia will be known in the annals of the world as the day of the world's most important medical discovery.

"May I not here recall the fact that after Congress passed the act establishing the National Hall of Fame at Washington, Georgia's Legislature created a commission to select the names of those two Georgians whose statues should be placed in that hall. This commission met in our State library, July 1, 1902, and chose the names of Crawford W. Long and Alex. W. Stephens as those to be thus distinguished. May we not all hope that our next general assembly will provide the necessary appropriation for the execution and fulfillment of this work.

"Too long we have permitted our people and his daughters to say of Dr. Crawford W. Long:

" ' "Though known to few, thy unrewarded fame was truly won,
Some day thy nation's heart shall proudly claim her gifted son."

" 'Mr. Chairman, it affords me great pleasure to tender this monument and medallion to the University of Georgia.' "